ABSTRACTS OF WORLD MEDICINE

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Hygiene and Public Health

1. **Proper Use of the Hospital in Treatment of the Aged Sick**
LORD AMULREE, A. N. EXTON-SMITH, and G. S. CROCKETT. *Lancet* [*Lancet*] **1**, 123–126, Jan. 20, 1951. 12 refs.

The treatment of the aged sick is one of the greater problems of the hospital and specialist services under the National Health Service in Great Britain. The final disposal of a group of aged sick patients in St. Pancras Hospital before the initiation of a new service, based on the hospital, to provide better facilities for the care of such persons is analysed and compared with the disposal of a series of patients admitted since the service was started. The two series are admittedly not strictly similar, but the general conclusion is drawn that much can be accomplished, given a certain enthusiasm in the medical and nursing attendants. A special point is made of the value of domiciliary visits, in the first instance before admission, and a plea is made for the greater encouragement of activity in aged patients while in hospital and the provision of hostel accommodation and other facilities to enable a quick turnover of the hospital population of aged sick to be attained.

Scott Thomson

2. **Thoughts on Housing for the Humid Tropics**
D. H. K. LEE. *Geographical Review* [*Geogr. Rev.*] **41**, 124–147, Jan. 1, 1951. 26 figs., 10 refs.

Housing shortages are not confined to cool climates but have been acute for many years in tropical areas where populations have increased and have tended to drift to the towns. The physiological principles underlying tropical housing are fully discussed, together with the need for using indigenous materials if costs are not to be excessive. As examples of what is being done, reports are quoted from India, East Africa, Nigeria, tropical Australia, and Puerto Rico. A series of excellent photographs of houses of desirable and undesirable types is appended. *G. M. Findlay*

3. **An Evaluation of Public-health Measures for the Control of Syphilis. An Epidemiological Study**
J. E. MOORE. *Lancet* [*Lancet*] **1**, 699–711, March 31, 1951; *American Journal of Syphilis, Gonorrhea and Venereal Diseases* [*Amer. J. Syph.*] **35**, 101, March, 1951. 22 figs., 26 refs.

This long paper, illustrated by many graphs which depict situations more vividly than is possible through the printed word, is the substance of the Malcolm Morris Lecture for 1950, delivered at St. Mary's Hospital, London.

It is established on reliable clinical grounds, but without statistical testimony, that the characteristics of syphilis have undergone a profound alteration during its 450 years of recognized history. Malignant destructive changes have been replaced by less obvious, but often more serious, lesions in the cardiovascular and nervous systems, and by latency. Indeed within the last 30 years in the U.S.A. the incidence of early asymptomatic neurosyphilis has declined from 25 to 40% to 5 to 15%, indicating that the change continues. No data other than recent are available for civil populations, but it is believed that the military incidence does to some extent mirror the situation of the district in which the troops are stationed. Graphs showing the figures for the Prussian, British, and United States armies are presented. In the Prussian army the combined incidence of chancroid and early syphilis declined from 30 per 1,000 in 1866 to 8·2 per 1,000 in 1911. In the British army the syphilis rate in 1890 was no less than 101·8 per 1,000, falling to 5·5 per 1,000 in 1924. In the American army, excluding troops stationed overseas, the rate was 40 per 1,000 in 1821 and rose to 73·2 per 1,000 after the Civil War (1861–5), but by the time of World War II it was as low as 5·9 per 1,000.

It is concluded, therefore, that during the period 1865 to 1910 there was a spontaneous decline in the incidence of fresh infections with syphilis in military personnel and, by inference, amongst civilians also. This was unrelated to public health measures since, before 1910, such control was almost non-existent apart from half-hearted and unsuccessful attempts to regularize prostitution. In any event this decline was also evident in the U.S.A. where regularized prostitution has never been considered an important factor in the spread of venereal diseases. It is possible that a change has occurred in the host–parasite relationship: indeed, a similar trend was noted in the figures for mortality due to tuberculosis even before the discovery of the tubercle bacillus and the institution of methods of control, and a similar decline has been noted in the seriousness of scarlet fever. On the other hand, it is considered more likely that the decline is principally associated with improved socio-economic status, for both mortality from tuberculosis and morbidity from syphilis have a higher incidence amongst unskilled persons. So far as syphilis is concerned, the Kinsey report showed that unskilled persons run the risk of infection 16 times more frequently than professional men. The rises in incidence that occur in wartime are not confined to countries actually fighting. A graph is presented which shows, during the period 1914 to 1918, the same rise in the

incidence of early syphilis, though at a lower level, in the neutral Dutch army as in the troops in France. It is postulated that a man has an approximately constant number of intercourses a year and that in war-time, when homes are broken and normal sexual alliances interrupted, he continues at his usual rate but that his consorts are of necessity more numerous. It is also pointed out that populations have been relatively more stable since 1910 and this fact may have contributed to a fall in the incidence since that time. Moreover, since 1910 effective treatment has been available and there are many civilian figures which show clearly the accelerated fall in incidence which followed after an inevitable time-lag of 8 to 10 years. The possible effect of penicillin in aiding the decline cannot be measured until another decade has passed, and the present decline is not sufficient to allow a relaxation of control methods.

In view of increasing transport facilities, syphilis can never be stamped out in one country while it still exists in another, and the problems of treating populations of the magnitude of those of India and China are so vast that the author does not believe that control will be achieved by treatment alone. He considers that research should be intensified and directed towards the goal of an immunizing vaccine. But until virulent treponemata can be successfully cultured no trials can be made.

[The author adopts a global viewpoint towards syphilis, and his comprehensive and interesting paper should be consulted in the original.] *R. R. Willcox*

4. Malaria Eradication Scheme, Mauritius

M. A. C. DOWLING. *Nature* [*Nature, Lond.*] **167**, 67–68, Jan. 13, 1951.

In 1949 an attempt was made to eradicate malaria in Mauritius, which has an area of 720 square miles (1,865 square kilometres) and a population of 450,000, by spraying the insides of buildings that harboured two malaria-carrying mosquitoes, *Anopheles funestus* and *A. gambiae*. The former breeds all the year round, the latter only in the hot season, January to May. The buildings (total 79,829) were sprayed with preparations of DDT and BHC, first from January to May and again from August to December. This was followed by a striking reduction in the incidence of malaria, the annual death rate, the infant mortality rate, and the number of mosquitoes. The mean annual death rate for 1934–48 per 1,000 population was $27{\cdot}2 \pm 3.37$, that for 1949 was 16·6; the infant mortality rate for 1934–48 per 1,000 live births was $150 \pm 19{\cdot}2$, that for 1949 was 91. The percentage reduction in the number of mosquitoes caught in dwellings was: *A. gambiae* 97·12, *A. funestus* 99·85, and *Aëdes aegypti* 99·94. The death rate from malaria during the epidemic first 6 months of the year was also much lower after the spraying; the mean rate for 1934–48 per 10,000 population was $32{\cdot}2 \pm 8{\cdot}07$; for 1949 it was 12·9, and for 1950, 4·9 per 10,000. Among 6,445 children born after the first spraying, only 15 (0·23%) had malarial parasites in the blood. *A. gambiae* bred profusely after the heavy rains of March and April, 1950, and as the malaria incidence continued to fall, it was believed that this mosquito, repelled by the insecticide on the walls, had altered its feeding habits and had found outside resting places. This view was strongly supported by experimental observation and the question is to be further investigated. *J. F. Corson*

5. DDT as a Residual Insecticide against *A. letifer* and *A. maculatus* in Malaya

C. P. NAIR. *Nature* [*Nature, Lond.*] **167**, 74–75, Jan. 13, 1951. 13 refs.

In a previous experiment made in the same hyper-endemic malarious village in Malaya, the inside and the outside of the walls of all the houses were sprayed with 5% DDT solution in kerosene, at the rate of 100 mg. per sq. ft. (1,076 mg. per sq. m.), 3 times between March and June, 1946. Practically no mosquitoes, *Anopheles letifer* being the chief vector, were caught for 2 to 4 weeks after each spraying. In the author's experiment a block of empty houses were similarly sprayed once only, and 2 people slept in each house for 14 days from the day of spraying; no mosquitoes were found among the dead insects collected daily in the houses. As kerosene repels mosquitoes for a few days only, any repellent effect was due to DDT, and the author believes that the mosquitoes which entered were irritated by the DDT on the inside walls and escaped. *A. letifer* is an " outdoor rester " and will also feed outside the houses. Another important malaria vector in Malaya is *A. maculatus*, which is also an outdoor rester though not an outdoor feeder. It was repelled to some extent when DDT was sprayed on outside walls only. The author considers that DDT can control *A. letifer* and malaria carried by it, and that it should be even more effective against *A. maculatus*. *J. F. Corson*

6. An Epidemic of Malaria in the Sahara. (Une épidémie de paludisme au Sahara)

R. HUGONOT. *Archives de l'Institut Pasteur d'Algérie* [*Arch. Inst. Pasteur Algér.*] **28**, 469–508, 1950. 18 figs., 28 refs.

The oasis of Beni Ounif-de-Figuig in the south of Algeria was at one period highly malarial. In 1907 drainage and other sanitary measures were instituted, with the result that malaria completely disappeared, and from 1926 to 1943 not a single case of malaria was recorded. It was thought that malaria had been completely abolished. From 1943 onwards more irrigation of gardens began to be practised and gradually slight differences in the system of raising water were introduced. In 1949, a year when the meteorological conditions were more particularly favourable, a widespread epidemic of malaria occurred, the insect vector being *Anopheles multicolor*. The infection was due to *Plasmodium falciparum* for the most part but some mixed infections with *P. falciparum* and *P. vivax* occurred. The infections with *P. vivax* especially were mild, possibly due to the admixture of negro blood. Neither proguanil nor chloroquine alone was satisfactory, but combined they were more effective.

[This epidemic shows that the only safeguard against the reintroduction of malaria in the tropics is eternal vigilance.] *G. M. Findlay*

7. Mortality from Circulatory Diseases in Norway 1940–1945

A. STRØM and R. ADELSTEN JENSEN. *Lancet* [*Lancet*] **1**, 126–129, Jan. 20, 1951. 4 figs., 3 refs.

Until the outbreak of war in 1940 there had been a rising mortality from diseases of the circulation in Norway. During the war there was a decline, with a quick return to former levels after the war. These trends were analysed for different age groups, different syndromes (apoplexy, arteriosclerosis, chronic nephritis, and chronic myocarditis), and for urban and rural populations. Bearing in mind the changing fashions in diagnosis, the authors nevertheless consider that there is evidence of a correlation between the incidence of circulatory disease and the composition of the diet, especially in respect of fats. Although the over-all decline was the same in rural as in urban districts, analysis of the mortality from the various syndromes showed that the decline was much less in rural districts in respect of arteriosclerosis and chronic myocarditis—the conditions which might be expected to be most affected by a reduction in fat intake, which was naturally more marked in the towns. *Scott Thomson*

8. Seasonal Incidence of Congenital Malformations of the Central Nervous System

T. MCKEOWN and R. G. RECORD. *Lancet* [*Lancet*] **1**, 192–196, Jan. 27, 1951. 3 figs., 10 refs.

The seasonal incidence of congenital malformations of the central nervous system has been investigated, two sources of information being employed: (1) the annual reports of the Registrar-General for Scotland, which have given the certified causes of stillbirths month by month since 1939, and (2) special observations made on 930 consecutive children born in Birmingham in 1940–47 with such malformations. The former data revealed a seasonal trend in the case of anencephaly, but not of other defects. The monthly rate of stillbirths attributed to anencephaly rose progressively from June to reach a maximum in the months of November to February and then fell off. For the 8 years 1939–46 the rate for the half-years April to September was 2·20 per 1,000 total births, and for October to March 2·83 per 1,000, a difference which is unlikely to be due to chance. The Birmingham data also revealed no significant seasonal variation in the incidence of spina bifida and hydrocephalus, but a substantial difference in the half-yearly rates of incidence of anencephaly—1·94 per 1,000 total births in the second and third quarters combined, and 2·70 per 1,000 in the fourth and first. In those cases where information on the length of gestation was available, the proportion conceived during the half-year from April to September was substantially greater for the children with anencephaly than for normal children. This seasonal variation cannot be explained simply in terms of seasonal changes in the relative proportions of first and of later births. No history of a specific fever during pregnancy was obtained from the mothers of the malformed children. The number of cases of malformation of the system among 470 sibs born after the birth of a child with such a malformation was 13, as against an expected number of approximately 2. *A. Bradford Hill*

INDUSTRIAL MEDICINE

9. New Liquid Skin Cleansers for Workers Exposed to Mineral Oil

L. N. SAVIDGE and F. H. TYRER. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **8**, 26–28, Jan., 1951. 6 figs., 1 ref.

Cleansers containing abrasives and those consisting essentially of solvents like kerosene are not recommended for regular use by workers whose skin is exposed to contamination with lubricating oils. Soap and detergents alone are comparatively inefficient. The authors admit that the most effective cleanser is probably a powder containing 50% wood flour, 48% powdered soap, and 2% borax. However, for subjects whose skin may become dry from very frequent use of this, or for those who prefer a liquid preparation, suitable mixtures of synthetic detergents and soap make effective and pleasant cleansers. Several formulae are given.

Scott Thomson

10. Bacterial Contamination of the Air in Boot and Shoe Factories

A. HIRCH. *British Journal of Industrial Medicine* [*Brit. J. industr. Med.*] **8**, 8–11, Jan., 1951. 6 refs.

The general bacterial count of the air was estimated in each of the 6 main working departments of 36 boot and shoe factories. The mean bacterial count was found to increase with increase in the number of workers in the room, that is, with increase in factory size; and there was also a significant, but less marked, decrease in the count with an increase in the area per worker.

There was a variation in the mean count between the different departments, the count in the clicking rooms being significantly higher than that in the other departments.—[Author's summary.]

11. Silicosis and Tuberculosis among Steel Foundry Workers. (Silicosi e tubercolosi nelle fonderie di acciaio)

E. ZANETTI and M. DOMPE. *Medicina del Lavoro* [*Med. d. Lavoro*] **41**, 321–368, Dec., 1950. 12 figs., 20 refs.

In steel foundries there is a high incidence of silicosis and tuberculosis, due largely to the quantity of dust present in the air when castings have to be freed from the mould. It is often necessary to use pneumatic tools to complete this process. Over 13,000 workers were studied, these being employed in 33 different works. Attempts were made to determine the incidence of silicosis and tuberculosis and to discover which processes were the most dangerous. The value of *x*-ray examination was also assessed.

Various kinds of material are used to make moulds, many having a high proportion of silica. If the parts to be made are small, as in chain works, the fragments of the moulds, as they are detached, fall through a grill on to a conveyer by which they are returned to the moulding shop. Much dust forms in this way. Larger castings can be freed from the covering mould only by attacking the latter with heavy hammers. Hollow castings may often require scraping of the interior with

small tools. Sometimes abrasive wheels are needed to clean and polish a casting and free it from adherent material. The mixing of the mould material does not involve much dust hazard, as it generally occurs in the open and the material may be wet. In general the methods of dust prevention are inadequate and the increasing use of pneumatic tools to clean the castings, though apparently unavoidable, much augments the risk.

In investigating the *x*-ray findings the authors used Vigilani's classification. Cases of silicosis were divided into five groups, while those with concomitant tuberculosis formed a sixth, which was subdivided into four groups of increasing severity. The workmen were classified in thirteen occupational groups, some of which are very much exposed to dust, others little exposed. The statistical estimation of the group incidence is made difficult by the changes of occupation within the industry. As was expected, the morbidity from silicosis and tuberculosis rose with length of employment. Radiographs were obtained in many cases from the industrial clinic or from the compensation office. Of 6,098 workers employed in the less hazardous jobs 493 had lung reticulation, 59 nodular silicosis, and 15 massive silicosis. Of the remaining 3,436 workers in more dangerous employment reticulation was present in 414, nodular silicosis in 140, massive silicosis in 62, and silico-tuberculosis in 22.

Five patients were selected for more detailed consideration; these were all men exposed to little dust. They had worked from 18 to 33 years in foundries. In 4 of them reticulation was evident and varied in degree; the bronchi showed up not by their translucency, but rather because they were surrounded by opaque material. Three cases were complicated by tuberculosis. In one case the development of this complication seemed to accelerate the silicotic process. In a second group of 6 persons more exposed to dust the *x*-ray findings varied considerably. In the first 3, silicotic changes progressed steadily, but were much less rapid in development when less dusty work was begun. The next 2 persons had associated tuberculosis in active form. The last patient also had tuberculosis with silicosis, but radiographic appearances changed little over a period of 3 years.

Preventive measures should include better ventilation and the separation of dusty from clean processes. Ventilating fans are often useful. All equipment not in use should be put away, and water-spraying of floors and other parts should be carried out freely. Cleaning and spraying should be done outside ordinary working hours. Totally enclosed machines could be more often used in mixing materials for the moulds, and the use of silicate should be cut down or stopped. Ventilation downwards is often preferable to upward aspiration. If this is associated with the free introduction of fresh air from above, the hazards are much reduced. There is much advantage in waiting until it has sufficiently cooled before removing a mould under a copious water spray, though this makes the process more lengthy and difficult, especially if pneumatic tools are used. In some works the mould is removed entirely by the use of water jets under high pressure (100 to 120 atmospheres). Pneumatic tools should have an attachment whereby the stream of dust is directed away from the operator by a rubber tube attached to the exhaust. When a furnace has to be demolished the dust hazard is very great and it is desirable to draw as much as possible downwards. Regular *x*-ray examination of personnel is needed and tuberculous subjects should be isolated. Of all persons examined 10·52% had reticulation and silicosis and 0·21% had associated tuberculosis. Tuberculous lesions were seen in 2·75%. *G. C. Pether*

12. **Tuberculosis among Native North African Workers Employed in the Industrial Fringe of Paris** (Remarques sur la tuberculose des ouvriers indigènes nord-africains travaillant dans la banlieue parisienne) P. DELAFONTAINE, G. DAMIENS, and R. DIACRE. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **27**, 89–92, Jan. 6, 1951.

In this article the authors discuss the medical and social factors contributing to the high incidence of tuberculosis among North African workers in Paris, and the clinical appearances and prognosis of the disease in these patients. In the Paris district the number of North Africans who are employed in local industries is estimated at 5% of the total population. The authors give no figures for the incidence of tuberculosis among them, but state that in one hospital one-quarter to one-third of the beds in the male tuberculosis wards are occupied by North Africans. Two main types of tuberculosis occur among these patients. One is an acute infection of the serous membranes—of the peritoneum as often as of the pleurae—and of hilar and cervical lymph nodes. The other is an ulcero-caseous pulmonary tuberculosis remarkable for the extent and gravity of the lesions. In some cases the diagnosis is uncertain owing to negative sputum findings and inconclusive radiographs, but when such patients are kept at rest and under observation for a few months the diagnosis of tuberculosis usually becomes more certain. The authors state that there is no racial tendency towards tuberculosis among these patients, all of whom are young men and 80% of whom are Berbers, but that the reasons for this high incidence of tuberculosis are mainly social. These North Africans, who are attracted to Paris by the prospect of high wages, are exposed to a colder climate than that to which they are accustomed, live in squalid conditions, eat insufficient food, work at heavy, unskilled labour, and send most of their wages home. They are often affected by amoebiasis and malaria.

Although the initial response to treatment, even with rest only, is good, the long-term prognosis is bad because the average North African has insufficient self-discipline and patience to continue the treatment. As long as he feels ill and is receiving active treatment, such as injections, he will remain in hospital, but as soon as he feels better he wants to leave. Many patients either take their own discharge against medical advice or have to be discharged for reasons of ward discipline. The same psychological factor operates with collapse therapy, for the North African cannot be relied upon to attend regularly for refills. Another factor is the long waiting

list for sanatorium treatment; usually the delay is of several months. During this period the North African, improved by his stay in hospital, considers himself cured and either resumes work or goes back to North Africa, where he loses the benefits of the French Social Security system and especially those benefits applying to diseases which need long-term treatment.

A. G. S. Heathcote

13. **Right Ventricular Hypertrophy in the Pneumoconiosis of Coalminers**

A. J. THOMAS. *British Heart Journal* [*Brit. Heart J.*] **13**, 1–9, Jan., 1951. 6 figs., 12 refs.

A study was made at the United Cardiff Hospitals of the degree of right ventricular hypertrophy to be found post mortem in 50 unselected cases of coal-miners' pneumoconiosis. Left and right ventricles were separated by dissection, weighed, and the ratio between them (LV/RV ratio) obtained. A significant reduction below the normal value of this ratio was found in 38 cases, indicating a high degree of right ventricular hypertrophy, the mean for the whole series being 1·16 (normal range 1·46 to 2·14). The lowest values occurred in cases in which there were massive pulmonary fibrotic lesions. In cases of massive emphysema with focal dust lesions there was much less tendency toward right ventricular hypertrophy and failure. It is suggested that the LV/RV ratio must be less than 1·00 before the electrocardiographic (ECG) pattern of right ventricular hypertrophy can be expected.

A total of 146 subjects, including 44 normal men, of whom 16 were miners, were also studied with regard to the ECG changes to be found in right ventricular hypertrophy due to pulmonary disease. It is stated that reduction in amplitude of R and increase in amplitude of S in lead V6 are the most prominent changes in such cases. Claim is also made for the value of a chest lead in the 3rd interspace just above V2 in indicating early hypertrophy of the right ventricular outflow tract. Cardiographic studies of respiratory variation following an exertion test are described. It is concluded that ECG evidence of right ventricular hypertrophy is not common in coal-miners' pneumoconiosis until the disease has advanced to the stage of massive fibrosis with infection, emphysema, and distortion.

L. W. Hale

14. **Roentgenographic Changes and Urinary Fluoride Excretion among Workmen Engaged in the Manufacture of Inorganic Fluorides**

E. J. LARGENT, P. G. BOVARD, and F. F. HEYROTH. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 42–48, Jan., 1951. 9 figs., 9 refs.

In the investigation described samples of urine from 23 workmen employed in a fluoride plant were examined for fluorides, and radiographs of all the bones of 16 of them were obtained. Positive *x*-ray findings in the form of abnormally dense bones were found in 5 cases. Changes were present in the pelvis and spine in each of these, and in some the extremities were also affected. There was a definite correlation between the urinary fluoride content and the occurrence of bone changes. Such changes may be expected if the concentration of fluoride exceeds 10 mg. per litre of urine.

None of the men with positive findings complained of any disability, nor did they show any *x*-ray evidence of hyperplastic changes in the spine like those described by Roholm and Shortt in Danish and Indian workers with fluorosis. The suggestion is made that the increase in bone density may make coincidental changes due to osteoarthritis more apparent, and that in consequence the part played by fluorides in causing limitation of mobility of the spine has been over-estimated by these workers.

J. A. Shiers

15. **Carbon Disulphide Hysteria.** (Sur l'hystérie sulfocarbonée)

M. J. ANDRÉ. *Archives des Maladies Professionnelles* [*Arch. Mal. prof.*] **12**, 9–18, 1951. 23 refs.

A case of chronic carbon disulphide poisoning is described in a man of 54 who had worked as a spinner in a viscose rayon factory for 2 years. He was found to have weakness of the middle, ring, and fifth fingers of the left hand, most marked in the muscles supplied by the ulnar nerve. There were no sensory changes at this stage. A year later, hypotonia of the flexor and extensor muscles of the left hand and diminished tendon reflexes in the left forearm were noted. By this time all forms of sensation in the distribution of the left ulnar nerve had nearly disappeared. A diagnosis of carbon disulphide polyneuritis was made. Two years later he had complete left hemi-anaesthesia, and voluntary movements were no longer obtainable in the left hand and wrist, which were held in the *main d'accoucheur* position. There were frank hysterical manifestations by this time, including bouts of apnoea followed by hyperpnoea.

The author emphasizes the difficulty of distinguishing signs of organic nervous changes from the hysterical features which are known to occur in this condition. He attaches importance to chronaxie measurements, which were carried out on three occasions during this patient's illness. These showed values lower than the normal for the flexors of the left hand and fingers, and values above normal for the extensors. The differences were not markedly consistent, however. An electroencephalogram revealed no abnormality. The author concludes that although carbon disulphide poisoning predisposes to hysterical nervous conditions, it can also give rise to a progressive polyneuritis, possibly due to the retention of carbon disulphide or its products in the body. He considers that chronaxie determinations are useful in detecting these organic changes.

John Pemberton

16. **The Porphyrins. The Significance of Porphyrins in Occupational Diseases**

C. P. MCCORD. *Industrial Medicine and Surgery* [*Industr. Med. and Surg.*] **20**, 185–190, April, 1951. 13 refs.

Anatomy

17. **The Superior Longitudinal Sinus and the Venous Drainage of the Surface of the Brain.** (Le sinus longitudinal supérieur et les voies de drainage de la convexité cérébrale)
A. DELMAS and J. CHIFFLET. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **26**, 4888–4894, Dec. 25, 1950. 6 figs., 26 refs.

An investigation was made, in 177 cases (109 male and 68 female subjects), of the superior longitudinal sinus to determine its circulation and that of the blood lakes adjacent to it, and to see whether the blood is carried into one or both lateral sinuses. In 42% only was the sinus truly sagittal, being a little to the left side in 25% and to the right in 32·5%. The mean length proved to be 22·8 cm., ranging from 17·5 to 26·5 cm. The mean calibre was 0·24 sq. cm. These measurements were found to have no relation to the size or shape of the skull, but bore a definite relation to the weight of the brain. The length was in direct proportion to the brain weight, and the cross-sectional area was in inverse proportion.

An analysis of the conformation of the torcular Herophili was also made. It was found to be of symmetrical type in 79·6%. In the majority of cases the right lateral sinus was larger than the left (66%) and the difference in size was associated with the lateralization of the superior longitudinal sinus or the straight sinus, variation in their calibre affecting the type of torcular Herophili. Thus Bailey's view that the superior sinus drains to the right lateral sinus and the straight sinus to the left applied only in a proportion of cases. The inference is that a jugulo-carotid anastomosis is as likely to revascularize the cerebral cortex when performed on the right as on the left side.

The afferents to the sinus are the frontal and occipital veins, which reach it directly; the Rolandic veins, which usually reach it by the intervention of the blood lake; and the parietal and occipital veins, which enter the external surface of the sinus.

The efferents other than the lateral sinuses form an important accessory path by osseous and meningeal routes. The marginal blood lakes vary in size with age. Also, these lakes vary in number, there being more in high, large skulls and especially in broad, capacious vaults. The suggestion is made that if the brain is large, a considerable part of the blood returns by these routes rather than by the sinuses, and that the venous blood lakes form a safety area. *Kenneth Bowes*

18. **Tissue Space and Plasma Circulation.** (Les espaces conjonctifs et la circulation plasmatique)
A. SALDANHA. *Bruxelles-Médical* [*Brux.-méd.*] **30**, 2289–2301 and 2346–2356, Nov. 5 and 12, 1950. 18 figs.

The author reviews his work on the injection of radio-opaque substances into connective-tissue spaces. When "lipiodol" is injected into the perivascular sheath of the neck of the human cadaver, it can be shown that there are in fact two sheaths, one around the artery, the other around the vein. The latter is narrow and difficult to inject. The peri-arterial sheath is continuous with that of the aorta and pulmonary arteries. These sheaths join an epicardial space lying between the myocardium and the visceral pericardium. The entire arterial system is in fact surrounded by a continuous perivascular sheath containing loose connective tissue and fluid. Outside the two perivascular sheaths in the neck there is another sheath, extending downwards into the thoracic inlet and coming into relationship with the thymus, the trachea, and the fibrous pericardium. In dogs it was possible to demonstrate a connexion between the perivascular sheaths and the more peripheral connective-tissue spaces. A system of channels extends from the peripleural spaces around the pericardium and on to the surface of the diaphragm. It reaches the peritoneal space and runs down around the thoracic and abdominal aorta. It is suggested that this system may be concerned in the spread of inflammation.

The interfascial spaces may form an intermediate circulatory system. They receive plasma from arterial capillaries and also tissue fluid, and come into close relationship with venous and lymphatic capillaries. Investigation of the physiological and pathological significance of the system is being continued.

R. Barer

19. **The Renal Arterial Vasculature in Man**
R. H. MORE and G. L. DUFF. *American Journal of Pathology* [*Amer. J. Path.*] **27**, 95–117, Jan.–Feb., 1951. 15 figs., 34 refs.

In this well-illustrated paper the authors give an account of the renal vasculature in the human kidney as studied by means of "neoprene" casts. These were made by injection and subsequent maceration of the surrounding tissues. As a result, Bowman's description of the vascular pattern was confirmed and evidence obtained supporting the theory of a juxta-medullary by-pass mechanism as put forward by Trueta and his co-workers.

Measurements were made, in a series of subjects of different ages, which provided the basis for a direct calculation of the capacity of the renal arterioles. In normal kidneys the authors were able to demonstrate only an occasional vessel directly by-passing a glomerulus, and therefore consider that such a mechanism is of no physiological importance. Sclerosed, hypertensive kidneys on the other hand showed many such by-passing channels, each of which probably represents the end result of an obliterative process in the glomerular capillary bed by means of which afferent arterioles are brought into direct connexion with efferent.

G. J. Cunningham

Physiology and Biochemistry

20. **Methionine Studies. I. Methionine Concentration in Human Serum Protein in Health and Disease and its Clinical Significance.** (Methioninstudien. I. Der Methioninspiegel im menschlichen Serumeiweiss Gesunder und Kranker und seine klinische Bedeutung)
D. MÜTING. *Zeitschrift für Klinische Medizin* [*Z. klin. Med.*] **147**, 478–492, 1951. 2 figs., 40 refs.

The mean proportion of methionine in the serum proteins of 120 healthy individuals was found to be 2·15%, with a range of 1·5 to 2·7%. Estimations were also made in 265 patients suffering from various diseases. In patients with liver disease the methionine content was found to be reduced, whereas in those with nephrosis, although the total serum protein content was reduced, the percentage of methionine was considerably raised. In patients with chronic nephritis the methionine content of the serum protein was normal or only slightly raised, and it is suggested that its estimation may help in the differentiation of nephritis from nephrosis.

J. R. Bignall

21. **The Duffy Blood Group System**
M. CUTBUSH and P. L. MOLLISON. *Heredity* [*Heredity*] **4**, 383–389, Dec., 1950. 1 ref.

Blood from a haemophiliac who had received a transfusion of incompatible blood was shown to contain 4 different isoantibodies, anti-A, anti-B, anti-D (Rh_0), and a hitherto undescribed antibody named, after the patient, Duffy, or anti-Fy^a. The antibody was eluted from the serum and the eluate used for testing other bloods. Thus an ABRh+ blood was found which did not react with eluate, and its erythrocytes were used to absorb the unwanted anti-A, anti-B, and anti-D from the original serum. The absorbed serum was tested in parallel with other available blood-group sera, none of which gave similar reactions. Of 205 samples of blood from unrelated English adults 65% reacted positively. The antigen detected is nominated Fy^a, and the hypothetical allelomorph Fy^b; the phenotype Fy(a+) includes bloods of both homo- and heterozygotes. The following gene frequencies were calculated: Fy^a 0·4075, Fy^b 0·5925. Family studies indicated that the antigen Fy^a is inherited. The antigen could be detected in blood from the umbilical cord of infants and from a 70-mm. foetus.

J. F. Loutit

22. **Agglutinin Anti-S in Human Serum**
H. I. COOMBS, E. W. IKIN, A. E. MOURANT, and G. PLAUT. *British Medical Journal* [*Brit. med. J.*] **1**, 109–111, Jan. 20, 1951. 1 fig., 11 refs.

The S antigen is closely related to the MN blood-group system. Reports have been published describing the occurrence of anti-S agglutinin in 6 cases, in 5 of which it was due to immunization by multiple transfusions, and in one to foetal incompatibility. Two unpublished cases are quoted in this paper, in one of which the anti-S agglutinin appeared to be a naturally occurring antibody. In a further case described by the present authors the anti-S agglutinin also seemed to be of natural occurrence and not the result of immunization. The patient was a woman of 54 who died in hospital from severe anaemia. Attempts at direct matching of her blood failed because an unusual agglutinin was present. This was identified as anti-S, but before compatible blood could be obtained the patient died. Subsequent investigations were carried out on blood obtained post mortem. This blood contained anti-S, but no anti-Rh, agglutinin and has therefore been valuable as a testing agent. The patient herself was S-negative, as were her husband and son (an only child born after 4 miscarriages) and 3 of her 6 siblings, but none other than the patient had anti-S in their serum. The patient had never had a blood transfusion, so that the anti-S factor was presumably of spontaneous origin.

M. C. G. Israëls

23. **Action of Thrombin in the Clotting of Fibrinogen**
K. BAILEY, F. R. BETTELHEIM, L. LORAND, and W. R. MIDDLEBROOK. *Nature* [*Nature, Lond.*] **167**, 233–234, Feb. 10, 1951. 11 refs.

24. **The Action of Oxygen and Carbon Dioxide on the Bronchioles and Vessels of the Isolated Perfused Lungs**
O. I. NISELL. *Acta Physiologica Scandinavica* [*Acta physiol. scand.*] Suppl. 73, **21**, 1–62, 1950. 26 figs., bibliography.

In animals, and to some extent also in man, an increase in the amount of carbon dioxide or a decrease in the amount of oxygen in the inspired air is known to cause pulmonary vasoconstriction. An investigation was carried out to determine whether such changes in the inspired air were also followed by alterations in the lumen of the bronchioles. Experiments were carried out on the isolated lungs of the cat (with one exception, when a rabbit was used), which were perfused with heparinized blood from the same animal and rhythmically inflated with gas mixtures of known composition.

If the bronchioles were in their usual state of dilatation, changes in the composition of the ventilating gas had no direct effect on their lumen. If, however, the bronchioles were constricted by muscarine (or drugs with a similar action) or by sympathetic stimulation, this constriction was inhibited both by lack of oxygen and an increase in the tension of carbon dioxide. It appeared that changes in the tension of both these gases acted directly on the bronchioles, and it is suggested that respiration might be assisted by this mechanism. It is also suggested that the development of bronchiectasis might be aided by anoxia in parts of the lungs, and that the beneficial effects of high altitudes on asthma or whooping-cough might be due to bronchiolar dilatation following upon anoxia.

E. M. Glaser

25. **Anatomical and Functional Structure of the Respiratory Centre.** (Structure anatomique et fonctionnelle du centre respiratoire)
O. A. M. Wyss. *Archivio Internazionale di Studi Neurologici* [*Arch. int. Studi neurol.*] **1**, 1–25, Dec., 1950. 2 figs., bibliography.

The author, who has made several contributions to our knowledge of the respiratory mechanism, reviews available information on the subject and builds up a picture of the respiratory centre.

The basic centre lies in the ventro-median nucleus of the bulbar reticular substance. It is autonomous and has a tonic inspiratory function, only achieving the normal automatic rhythm of respiration as a result of secondary modulation. This is brought about at three separate levels. First, an aggregation of cells in the bulbar reticular substance, lying dorso-lateral to, and enveloping, the tonic inspiratory centre, constitutes the primary expiratory centre, and when these two function together and alone, apneustic breathing is the result. The second inhibitory mechanism lies in a hitherto unlocated centre at the level of the pons (pneumotaxic centre), and the third is mediated by the vagus. Afferent fibres responding to inflation of the lungs relay in the cranial part of the nucleus of the tractus solitarius and pass to the primary expiratory centre. The main efferent tracts run from the inspiratory centre, in the first place to the 5th, 7th, 9th, 10th, 11th, and 12th cranial nerves, and secondly in the (mainly) homolateral antero-lateral tracts of the cord to the motor neurones responsible for the innervation of the respiratory muscles. Coordination is mainly achieved at the level of the inspiratory centre, but may also occur at spinal-cord level.

J. B. Stanton

26. **The Metabolism of Parenterally Administered Amino Acids. II. Urea Synthesis**
H. Kamin and P. Handler. *Journal of Biological Chemistry* [*J. biol. Chem.*] **188**, 193–205, Jan., 1951. 35 refs.

The maximum rate at which the dog can use the nitrogen of L-amino-acids for urea synthesis was studied by continuous infusion of various mixtures of amino-acids. The permeability of cells to the amino-acids was also investigated. Of the single amino-acids tested, glutamine and arginine formed urea most rapidly. It is suggested that glutamine occupies a central metabolic role in nitrogen metabolism. *H. M. Sinclair*

27. **The Amino Acid Requirements of Man. II. The Role of Threonine and Histidine**
W. C. Rose, W. J. Haines, D. T. Warner, and J. E. Johnson. *Journal of Biological Chemistry* [*J. biol. Chem.*] **188**, 49–58, Jan., 1951. 2 figs., 7 refs.

Previous work has shown that valine and methionine are indispensable dietary components for man. The same technique of nitrogen-balance determinations in subjects upon purified diets has now been extended to threonine and histidine. Removal of threonine from the diet rapidly caused a negative nitrogen balance which was abolished by feeding threonine. Threonine is therefore shown to be an essential component of the human diet. Removal of histidine from the diet had no effect upon the nitrogen balance. (This result was unexpected, since Rose had found that this amino-acid was required by all other species tested.) It is concluded, therefore, that histidine is not necessary for the maintenance of nitrogen equilibrium in normal adult man.

H. M. Sinclair

28. **Studies with Radiocalcium: the Intestinal Absorption of Calcium**
H. E. Harrison and H. C. Harrison. *Journal of Biological Chemistry* [*J. biol. Chem.*] **188**, 83–90, Jan., 1951. 8 refs.

It has previously been shown that rachitic rats treated with vitamin D absorb radioactive calcium more quickly than untreated animals. In the present work ^{45}Ca was administered by stomach tube to rats which were normal or made rachitic by a high-calcium, low-phosphorus diet. The most rapid rate of absorption occurred from the proximal portion of the small intestine within 2 to 4 hours and was unaffected by vitamin D. Some calcium was absorbed from the distal intestine.

It appears that vitamin D increases the efficiency of absorption of calcium only when the calcium of the intestinal contents is poorly soluble.

H. M. Sinclair

29. **Antagonism of Adrenocortical Extract and Cortisone to Desoxycorticosterone: Brain Excitability in Adrenalectomized Rats**
D. M. Woodbury, J. W. Emmett, G. V. Hinckley, N. R. Jackson, J. D. Newton, J. H. Bateman, L. S. Goodman, and G. Sayers. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **76**, 65–68, Jan., 1951. 2 figs., 7 refs.

It has been shown that adrenal cortical extract (ACE) and cortisone will counteract the depressive effect of deoxycortone acetate (DCA) on brain excitability in intact rats. The present report concerns the effects of ACE and cortisone on adrenalectomized rats after implantation of DCA. Adult male Sprague–Dawley rats were used and the " electroshock threshold " (EST) was determined by the technique described by Davenport (*Amer. J. Physiol.*, 1949, **156**, 322). Some of the rats were then subjected to adrenalectomy and 6 15-mg. pellets of DCA implanted, some were left intact but DCA implanted, and some served as untreated controls. The EST of the intact DCA-implanted rats increased compared with that of the controls, and that of the adrenalectomized DCA-implanted animals increased even more markedly. Both ACE and cortisone reduced the elevated EST of the adrenalectomized DCA-implanted rats; the degree of reduction was not, however, related to the loss of body weight. On withdrawal of the hormones the EST slowly increased to its original level.

These observations support the theory that DCA acts by antagonizing cortisone-like steroids at their site of action rather than by inhibiting pituitary release of adrenocorticotrophin (ACTH), since in the adrenalectomized animals the endogenous secretion of cortical steroids was *nil*. The authors suggest that the chemically

similar DCA and cortisone compete for the same strategic loci in the cell. The test animals responded more rapidly to cortisone and ACE treatment if given water to drink instead of sodium chloride solution, suggesting a relationship between EST and the extracellular sodium level.

The possibility that brain-excitability determinations may be useful as a method of assaying cortisone-like compounds is being explored. *Nancy Gough*

30. **Influence of Adrenaline and Insulin on Adrenal Cortical Response to ACTH**

C. FORTIER, F. R. SKELTON, and P. CONSTANTINIDES. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **76**, 77–78, Jan., 1951. 8 refs.

It has been shown that ingestion of glucose enhances the response of hypophysectomized animals to adrenocorticotrophin (ACTH), suggesting that the blood sugar level affects the action of ACTH on the adrenal cortex. This paper records the results of a study of adrenal cortical response to ACTH in hypophysectomized male rats under conditions of adrenaline-induced hyperglycaemia and insulin-induced hypoglycaemia. Determinations of blood glucose, adrenal cholesterol and ascorbic acid, plasma ascorbic acid, and liver glycogen concentrations were made by standard methods. ACTH was injected subcutaneously, followed by adrenaline and insulin at intervals of 60 and 90 minutes respectively, so that the full action of ACTH coincided with the maximum hyper- and hypoglycaemic levels. Hypophysectomized rats receiving ACTH, insulin, or adrenaline alone were killed at corresponding time intervals for comparison.

Changes in blood sugar level induced by insulin or adrenaline were not influenced by ACTH administration. Moreover, neither adrenaline nor insulin modified the effect of ACTH on the liver glycogen and adrenal cholesterol and ascorbic acid levels. Hence hyperglycaemia *per se* does not enhance the action of ACTH on the adrenal cortex; the effect of alimentary hyperglycaemia must be attributed to an increase in the total store of carbohydrates or to an excess production of intermediary metabolites. *Nancy Gough*

31. **Strength and Endurance in the Waking and Hypnotic States**

E. S. ROUSH. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 404–410, Jan., 1951. 1 fig., 10 refs.

Twenty subjects who achieved amnesic somnambulism under hypnosis were examined to determine whether physical strength is increased in the hypnotic and post-hypnotic states. Three tests were applied: an arm-dynamometer test, a hand-dynamometer test, and an endurance test consisting in hanging by the hands from a bar. In a first series of experiments increased strength under hypnosis was established for the arm-dynamometer test only, the average increase being 16·8%, which was found to be statistically significant. In a second and more elaborate series of experiments the inhibitory effect of pain on physical performance was eliminated by hypnotic suggestion. Under these conditions a statistically significant rise of hypnotic performance was obtained in all three tests; the two dynamometer tests also indicated a significantly improved post-hypnotic performance. *F. K. Taylor*

32. **The Theory of Cerebral Localization**

W. GOODDY and W. MCKISSOCK. *Lancet* [*Lancet*] **1**, 481–483, March 3, 1951. 10 refs.

33. **Direct Measurement of Renal Vessel Pressures under Stress of Acceleration**

S. W. AMES, S. ROSENFELD, and C. F. LOMBARD. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 399–403, Jan., 1951. 1 fig., 5 refs.

The renal vessels of 10 young goats were cannulated and the venous and arterial blood pressures measured during repeated 15-second exposures to positive and negative accelerating forces of 2 and 3 *g*. In the case of positive acceleration an initial rise in renal arterial and venous pressures occurred, after which, at 2 *g*, the arterial pressure fell steadily and the venous rose slightly, while at 3 *g* the arterial pressure fell as before, but the venous pressure fell at first, often to a subatmospheric level, and then gradually rose to the pre-exposure level. On termination of the acceleration arterial pressure rose steeply to above the initial level and venous pressure returned to the initial level. The pulse slowed slightly during acceleration and markedly afterwards. On exposure to negative acceleration a fall in both arterial and venous pressures occurred at the outset and persisted throughout the exposure; on termination of the exposure arterial and venous pressures rose above the initial levels and gradually returned to normal. The pulse rate fell during exposure and increased after it

It was concluded that the changes in renal blood pressure induced by both positive and negative acceleration are sufficient to depress renal function, and probably reduce the urinary output. *D. H. Sproull*

34. **Effect of Adding Carbon Dioxide to Inspired Air on Consciousness Time of Man at Altitude**

F. G. HALL and K. D. HALL. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **76**, 140–142, Jan., 1951. 2 figs., 6 refs.

The average duration of useful consciousness at a simulated altitude was determined by the senior author's method in 9 young adults whose pulmonary ventilation was recorded photokymographically. At a simulated altitude of 30,000 feet (9,140 m.; 226 mm. Hg) average duration of useful consciousness increased from 88 seconds to 163 seconds when a mixture containing 21% oxygen, 14% carbon dioxide, and 65% nitrogen was substituted for atmospheric air. At 35,000 feet (10,670 m.; 179 mm. Hg) a similar increase occurred, but was less pronounced, when a mixture containing 21% oxygen, 19% carbon dioxide, 60% nitrogen was substituted for air. In both cases the prolongation of useful consciousness was attributable to increased ventilation.

J. E. Cotes

Pharmacology and Therapeutics

35. **Differences in the Concentration of Chloroform in the Blood of Man and Dog during Anesthesia**
L. E. MORRIS, E. L. FREDERICKSON, and O. S. ORTH. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **101**, 56–62, Jan., 1951. 3 figs., 27 refs.

Details are given of a method of estimating chloroform in blood by a modification of the Fugiwara test. To 2 ml. of venous blood is added 18 ml. of diethyl ether and, after shaking, 5 ml. of the supernatant is removed. To 2 ml. of 20% sodium hydroxide in calibrated colorimeter tube, 5 ml. of pyridine is added, the 5 ml. of supernatant layered on top, the tube fitted with a reflux condenser, and the whole put in a bath at 82° C. for 8 minutes. The volume is made up to 12 ml. with ethyl alcohol after cooling, and the colour intensity compared in a colorimeter with a standard. In dogs in which chloroform anaesthesia was well established the blood chloroform level ranged from 18 to 50 mg. per 100 ml. In 67 samples from 58 patients receiving chloroform alone for general anaesthesia the level ranged from 2·0 to 23·2 mg. per 100 ml. (mean 9·2). During first-plane anaesthesia (Stage III) the mean figure was 7·1 mg. per 100 ml.; during Plane 2, 10·6 mg. per 100 ml.; during Plane 3, 12·2 mg. per 100 ml.; and during Plane 4, 16·5 mg. per 100 ml. In 53 patients receiving 60 to 70% nitrous oxide in addition to chloroform the mean level was 8·8 mg. per 100 ml. Some 30 to 50% of the chloroform administered is eliminated in 15 minutes, but complete elimination may take 8 hours. The mean figures for blood chloroform levels in dogs are thus considerably higher than in man for comparable degrees of anaesthesia. Species difference in reaction to this, as to many drugs, is thus in evidence. *James D. P. Graham*

36. **Effect of Barbiturate Anesthesia on Potassium Metabolism of the Rabbit and Dog**
J. M. STEWART. *American Journal of Physiology* [*Amer. J. Physiol.*] **163**, 622–632, Dec., 1950. 4 figs., 16 refs.

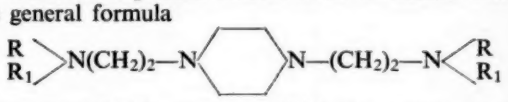
In rabbits and dogs anaesthetized with pentobarbitone (" nembutal ") or allobarbitone (" dial ") the plasma potassium level was reduced by 7 to 37%. In rabbits the urine volume and the urinary concentration, total excretion, and clearance of potassium rose during the first 3 hours after administration of either drug. In dogs dial had similar effects, but nembutal caused a small initial fall and a later rise in plasma potassium level, a diuresis, and increased potassium excretion. After an intraperitoneal injection of potassium chloride (300 mg. per kg. body weight), anaesthetized rabbits showed a slow rise in plasma potassium level up to 140% of normal, without death; urine volume and excretion and clearance of potassium were all increased, and 28% of the injected potassium was excreted in 3 hours. Under dial anaesthesia the injection resulted in an immediate increase in plasma potassium level up to 263% of control values, and 3 out of 4 animals died; the urine volume and excretion and clearance of potassium increased at first, but fell later to low levels, so that only 14% of the injected potassium was excreted in 3 hours. The increase in plasma potassium concentration during anaesthesia was considered to be due to a diminished uptake of potassium by body cells. *R. A. Gregory*

37. **Muscarinic, Nicotinic, and Curarizing Properties of Alkyldimethylaminoethanols.** ((Propriétés muscariniques, nicotiniques et curarisantes des alkyl-diméthyl-amino-éthanols)
M. J. DALLEMAGNE and E. PHILIPPOT. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **84**, 189–208, Dec., 1950. 10 figs., 11 refs.

The alkyldimethylaminoethanols may be regarded as derivatives of choline, one of its methyl groups being replaced by $C_{2n}H_{2n+1}$, the value of n ranging from 1 to 9. The relative potency of these substances in respect of their muscarinic, nicotinic, and curarizing effects has been determined in cats and dogs. Their muscarinic activity was found to be less than that of choline, and absent in the octyl and higher derivatives. Nicotine-like stimulant action was greatest in the C_6 compound, while ganglionic blocking activity increased up to the C_{10} compound and then decreased. This action, in the longer-chain derivatives, was prolonged. Adrenaline-potentiating action was possessed by all the substances, but especially by the C_6, C_{12}, and C_{16} compounds. Curarizing activity was greatest in the C_{12} compound; respiration was arrested, but recovered, this respiratory depression being believed to be partly secondary to the fall of blood pressure which the drug causes. *Derek R. Wood*

38. **Curarizing Activity of Quaternary Ammonium Derivatives of Certain New Tetramines.** (Activité curarisante d'ammoniums quaternaires dérivés de nouvelles tétramines)
R. HAZARD, J. CHEYMOL, P. CHABRIER, E. CORTEGGIANI, and F. NICOLAS. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **84**, 237–256, Dec., 1950. 4 figs., 11 refs.

The authors have investigated the curarizing activity in animal preparations of a number of quaternary ammonium compounds derived from tetramines having the general formula



These compounds are all soluble in water. It was found that the presence of the piperazine nucleus was associated with increased curarizing activity by comparison with compounds which lack it. The most active compounds were those in which there was a piperidyl group at R, and the derivatives with an ethyl group at R_1 were more active than those with a methyl group at that

site. The iodide was generally more active than the bromide, chloride, or the CH_3–C_6H_4–SO_3–derivative. The activity of each compound was compared with that of D-tubocurarine by the rabbit head-drop method and on the rat phrenic-nerve–diaphragm preparation and the frog (isolated rectus abdominis muscle and whole animal). In addition, the effects on blood pressure in the dog and on cholinesterase activity were observed. These experiments showed the most active of the compounds tested to be bis-(piperidyl)-piperazine diethiodide (336HC), which is to be given clinical trial in man. By the head-drop test it was 15 times less active than D-tubocurarine, but its toxicity in mice was 66 times less. It had no appreciable effect on the blood pressure. The ratio between the dose of 336HC causing respiratory or cardiac arrest and that causing head-drop was greater than with D-tubocurarine. The authors emphasize the need to use a standard test in comparing the curarizing activities of drugs, and reiterate their belief that the rabbit head-drop test gives a better indication of therapeutic usefulness than the other methods in common use.

Derek R. Wood

39. **Human Pain Thresholds Determined by the Radiant Heat Technique and the Effect upon Them of Acetylsalicylic Acid, Morphine Sulfate and Sodium Phenobarbital**

R. A. KUHN and R. B. BROMILEY. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **101**, 47–55, Jan., 1951. 1 fig., 11 refs.

Determinations were made of the pain threshold to radiant heat applied to a blackened area of skin on the forehead for a period of 3 seconds every 3 minutes in normal human subjects, using the Hardy–Wolff–Goodell apparatus. An initial stimulus of 100 millicalories was applied and a threshold determined by increasing this intensity by steps of 50 millicalories until pricking pain was reported, the mid-point between the intensities of stimulus which just caused and just failed to cause a painful sensation being taken as the " rough threshold ". Six determinations were then made at each of 5 intensities —the rough threshold level and 10 and 20 millicalories above and below it—the order of testing being random and tests being made at other intensities if necessary. In 37 subjects so tested the variation in " normal " threshold was considerable, the range being from 169 to 296 millicalories and the mean 232·2 (S.D. 31·9).

The 50% pain threshold was then determined in 15 fasting subjects before and after taking 0·9 g. of acetylsalicylic acid and the results compared with those in 10 control subjects who were given sucrose, with due precautions as to avoidance of selection, concealment from both recorder and subject, the Reed and Muench formula being used for calculation of the 50% threshold. There was no statistically significant difference between the two determinations in either group. Similar experiments were performed to determine the effect of subcutaneous administration of 0·016 g. of morphine sulphate (8 subjects) and of 0·096 g. of sodium phenobarbitone (4 subjects). Both groups experienced some dizziness, and the latter were also sleepy. Very wide differences in the response to morphine occurred, the 50% pain threshold after the drug varying from 1·5% below the initial value to above the level for tissue damage. The effect of phenobarbitone appeared negligible. The authors note that these findings differ markedly from those of Wolff *et al.* and attribute this to the use of inadequate methods of pain-threshold determination by these workers.

James D. P. Graham

40. **Clinical Evaluation of Analgesic Drugs. A Comparison of Nu-2206 and Morphine Sulfate Administrered to Postoperative Patients**

R. S. JAGGARD, L. L. ZAGER, and D. S. WILKINS. *Archives of Surgery* [*Arch. Surg., Chicago*] **61**, 1073–1082, Dec., 1950. 4 refs.

The analgesic efficacy of " Nu 2206 " (3-hydroxy-N-methylmorphinan hydrobromide) in the treatment of post-operative pain was compared with that of morphine sulphate in 642 patients in the general and urological surgical wards of the University of Iowa Hospitals. The patients were divided into groups according to the region of the operation, and each was given either morphine or Nu 2206 by subcutaneous injection every 3 hours, provided he requested it, for 5 days after operation. Of those given morphine sulphate, 251 were given doses of 10 mg. and 87 of 5 mg., and of the remainder, 218 were given doses of 5 mg. and 86 of 2·5 mg. of Nu 2206.

Since the average number of doses of either drug required during the 5-day period was only 3·4, no accurate comparison could be made of their duration of action. There was no significant difference between the average number of doses of morphine and Nu 2206 given at the higher dose levels, but at the lower levels the number of doses of morphine was greater. There was a greater tendency for side-effects to occur with Nu 2206 than with morphine. More doses of morphine than of Nu 2206 were required after renal operations, while the reverse was true after operations on the spinal column. Patients who underwent deep thoracic, spinal-column, and renal operations required the most analgesia, but there was a decline in requirements during the 5 days after all operations except those on the spinal column.

P. A. Nasmyth

41. **The Action of Morphine, Pethidine, and Amidone upon the Intestinal Motility of Conscious Dogs**

E. M. VAUGHAN WILLIAMS and D. H. P. STREETEN. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 584–603, Dec., 1950. 10 figs., bibliography.

Using methods described in earlier papers, the authors have investigated the effects of analgesic drugs on the activity and propulsive power of Thiry–Vella loops in dogs. The technique enables the activity of each end of the loop, the volume of the loop, and the volume of fluid propelled against a known pressure to be measured. The experiments were performed on 8 dogs trained to lie quietly and from which food had been withheld overnight. Morphine injected subcutaneously in doses

of 30 mg. or more per kg. body weight reduced activity and for a time abolished the propulsion of fluid through the loop. This was accompanied by a diminution in the volume of fluid in the loop, showing that continuous contraction rather than absence of contraction was the cause of the failure to propel fluid.

The effect of each drug on the activity of the loop was assessed by determining the threshold dose, which was taken as the mean of two doses, one which did, and one which failed to, arrest the propulsion of fluid for 5 minutes. The threshold was 29 mg. per kg. for morphine (sulphate), 77 mg. for amidone (hydrochloride), and 1·7 mg. per kg. for pethidine (hydrochloride). A second comparison was made by calculating the difference between the work performed by the loop in a control period with that performed during the action of the drug (work being the product of the weight of fluid transferred and the height it was raised). Dose–response curves were constructed which showed ratios of activity of the drugs very similar to those obtained from comparison of threshold doses. On the basis of figures for analgesic activity as given in the literature, amidone and pethidine were calculated to have advantages of 5 : 1 and 75 : 1 over morphine when analgesia without interference with the propulsive power of the intestine is required.

The effects and mode of action of morphine on the intestine are considered at some length.

R. P. Stephenson

42. **Action on Experimental Haemorrhagic Shock in Dogs of 3885 R.P. (1-Ethanesulphonyl-4-ethyl-piperazine).** (Action de l'éthane-sulfonyl-1 éthyl-4 pipérazine (3,885 R.P.) sur le choc hémorragique expérimental du chien)
J. Fournel and P. Dubost. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*[**84**, 283–307, Dec., 1950. 6 figs., 38 refs.

43. **Effect of Halogenated Ethylamines on Cardiac Arrhythmias Induced by Epinephrine, Nicotine and Cyclopropane**
V. A. Drill and H. W. Hays. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **101**, 74–81, Jan., 1951. 3 figs., 7 refs.

Dogs were given a preliminary injection of thiopentone, and anaesthesia was then maintained with 16% cyclopropane while records of blood pressure and respiration and electrocardiograms were taken. Adrenaline was injected at a constant rate in a dosage of 1 μg. per kg. body weight per 20 seconds until cardiac arrhythmia appeared, the dose required ranging from 0·6 to 4·7 μg. per kg. The administration of a test dose of 0·25 to 0·5 mg. of nicotine similarly induced temporary arrhythmia, while in half the dogs an increase in concentration of the cyclopropane to 35 or 40% also caused arrhythmia, the remainder developing ventricular ectopic beats only under deep cyclopropane anesthesia or during the ensuing apnoea. After these control tests, an injection of one of three synthetic adrenergic blocking agents was given and the tests repeated. The compounds used were N-(2-bromoethyl)-N-ethyl-1-naphthalene methylamine (" SY 28 "); N-[2-(2-biphenylyloxy)-ethyl]-N-(2-chloroethyl) butylamine) (" SY 30 "); and N-(2-chloroethyl)-N-ethyl-9-fluorenylamine (" SY 21 "). All 3 compounds suppressed the arrhythmia induced by adrenaline, nicotine, or excess cyclopropane to an equal degree, but SY 30 caused less fall in blood pressure than the others and, in doses which blocked arrhythmia, did not reverse the pressor response to adrenaline. Control studies showed that nicotine itself would fail to produce arrhythmia after 3 doses had been injected, at which time blood-pressure responses were still marked.

James D. P. Graham

44. **Effect of Ouabain on the Coronary Circulation and Other Circulatory Functions in Intact Anesthetized Dogs**
R. G. Page, E. L. Foltz, W. F. Sheldon, and H. Wendel. *Journal of Pharmacology and Experimental Therapeutics* [*J. Pharmacol.*] **101**, 112–118, Jan., 1951. 1 fig., 9 refs.

Techniques have recently been perfected for measuring cardiac output, coronary flow, and cardiac oxygen consumption in anaesthetized dogs, so that it is possible to study the effects of drugs on the heart more closely than by means of blood-pressure records and electrocardiograms alone. The effects of two doses of ouabain (0·026 mg. per kg. body weight, or 1/3 LD50; and 0·037 mg. per kg., approaching the toxic dose) were investigated on a total of 17 animals. The lesser dose produced little significant effect on the heart other than an increase in coronary resistance. The higher dose caused slowing of the heart from increased vagal tone, arrhythmia (in most of the animals), a rise in systemic blood pressure, and a decrease in coronary flow. The coronary resistance, work done by the heart, and its O_2 consumption were increased, and the pulmonary arterial pressure fell. The decreased coronary flow might be due to vasoconstriction in the coronary vascular bed or to increased diastolic tone in the heart. That it was not due to the slowing of the pulse is indicated by the rise in cardiac O_2 consumption. The mechanical efficiency of the " normal " heart was thus improved in the dogs given ouabain, as compared with anaesthetized control dogs, but the decrease in coronary flow must be regarded as an unfavourable factor in relation to the increased work done by the myocardium against a higher mean aortic pressure. In a failing heart, when output might be expected to rise, this unfavourable aspect would be much lessened.

James D. P. Graham

45. **The Hypotensive Action of Protoveratrine**
S. W. Hoobler and R. W. Corley. *University of Michigan Medical Bulletin* [*Univ. Mich. med. Bull.*] **16**, 362–368, Nov., 1950. 2 figs., 10 refs.

Protoveratrine (an alkaloid of *Veratrum album*, or white hellebore) was given intravenously to 51 hypertensive patients in doses of the order of 0·14 μg. per kg. In 40 the drug produced a significant fall in blood pressure, reducing by more than 20 mm. Hg the mean of systolic and diastolic pressures. This effect was maximum some 10 to 15 minutes after the injection, and had

usually largely passed off at the end of 30 minutes. Side-effects were not serious: nausea and vomiting, dizziness in a few cases, and occasional flushing. In all cases the pulse slowed to a variable degree; this could be prevented by atropine. It was thought that there was a hypotensive effect beyond that due to the bradycardia, as there was evidence of diminished peripheral resistance; the drug increased blood flow to the limit in all 17 patients in whom records were made of blood flow to the forearm or leg. In some patients whose hypertension was unrelieved by sympathectomy there was a satisfactory hypotensive response to the drug both before and after operation.

Thus protoveratrine was not helpful in deciding which hypertensive patients might respond to sympathectomy. Its effect, when given intravenously, was too brief to have any therapeutic value, except possibly in hypertensive crises. *J. A. Cosh*

46. **Studies on the Effects of Parenteral Quinidine Administration**

H. BINDER, J. BURSTEIN, W. HOROWITZ, E. GERSH, and R. SMELIN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **86**, 917–933, Dec., 1950. 3 figs., 17 refs.

In 15 normal subjects and 15 with heart disease but normal rhythm intramuscular injection of 0·65g. quinidine lactate caused a maximal lengthening of the Q–T segment in 30 minutes. The effect remained about the maximum for 2 to 4 hours, and was just detectable after 24 hours. In 8 cases of supraventricular tachycardia one or more intramuscular injections of quinidine lactate caused slowing of the auricular rate in 2 and reversion to sinus rhythm in 6 cases. In 3 cases of auricular flutter 0·65 g. slowed the auricular rate. Sinus rhythm was restored in 5 out of 6 cases of auricular fibrillation by one or more intramuscular injections of 0·65 g. In 2 cases of Wolff–Parkinson–White syndrome normal conduction was restored for 2 to 3 hours. In 3 cases of ventricular tachycardia the ventricular rate was slowed, and in one case nodal tachycardia occurred.

Intravenous injection was followed by severe toxic reactions in each of 7 normal subjects. In several of the patients with irregular rhythm intravenous injection had a similar effect to intramuscular, with earlier onset and shorter duration.

Quinidine lactate intramuscularly was no more toxic than quinidine by mouth. It is suggested that 0·65 g. may be given hourly in urgent cases.

D. Verel

47. **The Effects of Hexamethonium Bromide on the Stomach**

A. H. DOUTHWAITE and M. G. THORNE. *British Medical Journal* [*Brit. med. J.*] **1**, 111–114, Jan. 20, 1951. 8 figs., 2 refs.

Kay and Smith (*Brit. med. J.*, 1950, **1**, 460) showed that in the stomachs of patients with duodenal ulcers hexamethonium iodide ("C6") completely inhibited the spontaneous secretion of hydrochloric acid, and that it reduced the secretory response to insulin-produced hypoglycaemia, but did not affect that produced by histamine. They also found that C6 caused a prolonged inhibition of gastric motility.

The present authors have studied the effect of C6 on 10 patients in bed (9 of whom had duodenal ulcers), using the barium meal and the gruel test meal. Radiographs showed that after C6 (100 mg. intramuscularly) the onset of gastric emptying was delayed up to 30 minutes in some cases, and that complete emptying of the stomach was delayed for up to 6 hours. Gastric peristalsis, although diminished, was not completely arrested, but the small gut was dilated and immobile for up to 6 hours after the injection of C6. Secretion of acid was only slightly diminished, if at all, except in one case where it was completely abolished; this lack of inhibition might be due to the secretion being hormone-induced rather than vagus-induced.

Marked side-effects were observed, chiefly arising from loss of vascular tone; 6 patients fainted while standing up to take the barium meal. The authors suggest that C6 may be of use in the treatment of gastric and duodenal ulcer, chiefly in patients in bed and at night, when the side-effects would be minimal.

John R. Vane

48 (*a*). **The Quantitative Analysis of Antral Gastric Motility Records in Normal Human Beings, with a Study of the Effects of Neostigmine**

N. C. HIGHTOWER and C. F. CODE. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **25**, 697–704, Dec. 20, 1950. 3 figs., 9 refs.

The changes in pressure in a small, water-filled balloon resting in the gastric antrum and connected to a manometer were recorded on photographic paper, thus providing an indication of gastric motility in normal subjects. The terminology first used by Templeton and Lawson (*Amer. J. Physiol.*, 1931, **96**, 667) in describing large-intestine motility was adapted to the description of the motility patterns observed, in which three characteristic types of wave were distinguished. Type-I waves were of low amplitude (5 cm. H_2O) and, when rhythmic, occurred at a constant rate of $2{\cdot}9 \pm 0{\cdot}08$ per minute. They were present, on average, for 23% of the period of observation, and were of a rhythmic nature for 13% of that time. Type-II waves only differed from Type I in degree and rate of pressure-change produced. The rise and decline in pressure was rapid; pressures up to 100 cm. H_2O were recorded, but the usual range was 10 to 50 cm. H_2O. They were present for 15% of the time and were rhythmic (3 per minute) for 5%, their mean duration being 12 to 14 seconds. Type-III waves were present for only 1% of the time and consisted of a series of rhythmic Type-II waves superimposed upon an elevation of basal pressure up to 10 cm. H_2O, varying in duration from 2 to 5 minutes. In 11 subjects the intramuscular injection of neostigmine (0·5 mg.) produced a slight increase in the duration and height of the non-rhythmic Type-II waves.

[The percentages were estimated by summating the durations of each type of wave and expressing this figure as a percentage of the total time of observation.]

John R. Vane

48 (*b*). **The Effects of Urethane of *beta*-Methylcholine Chloride ("Urecholine") on Antral Gastric Motility in Man following Vagotomy**
N. C. HIGHTOWER, W. WALTERS, and C. G. MORLOCK. *Proceedings of the Staff Meetings of the Mayo Clinic* [*Proc. Mayo Clin.*] **25**, 705–710, Dec. 20, 1950. 1 fig., 16 refs.

The method employed in the previous paper (Abstract 48 (*a*)) was used in studying the effects of β-methylcholine chloride ("urecholine") upon gastric antral motility in 13 patients who had undergone vagotomy for peptic ulcer (8 patients had also undergone gastroenterostomy). After a control period of one hour, 5 mg. of urecholine was injected subcutaneously and the recording continued for an hour. The effect of the drug was seen after an interval which varied from 1 to 17 minutes (mean 6 minutes), and lasted throughout the observation period. Type-I waves were present 21% of the time before urecholine was given and 37% after, but this difference was not significant ($p=0{\cdot}1$). The mean proportion of time during which Type-II waves were present increased from 6 to 22%, and the mean pressure change increased from 9 to 20 cm. H_2O, both changes being significant ($p=0{\cdot}05$). The rhythmic rate of waves of Types I and II was not altered. Type-III activity was observed only once before and 5 times after urecholine administration.

The commonest of the few side-effects produced by urecholine was found to be mild abdominal cramp. In all, urecholine increased the periods of activity from 27 to 59% of the time of observation. As the rate of activity of types 1 and II was the same in patients after vagotomy as in normal subjects (3 per minute) it is suggested that this represents a fundamental type of motor activity of the gastric antrum. *John R. Vane*

49. **An Evaluation of Adrenergic Blocking Agents.** [In English]
G. CHEN, V. L. NASH, and D. RUSSELL. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **84**, 269–275, Dec., 1950. 3 figs., 10 refs.

50. **Observations on the Effects of the Autonomic Blocking Agent, Bis-trimethylammonium Pentane Dibromide (C5) in Normal Subjects and in Patients with Peripheral Vascular Disease and Hypertension, and Comparison with Tetraethylammonium Chloride**
D. GROB and A. MCG. HARVEY. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **87**, 616–639, Dec., 1950. 4 figs., 27 refs.

The actions of tetraethylammonium (TEA) and bis-trimethylammonium pentane (pentamethonium; "C5") compounds have been widely studied, and the present observations on normal subjects and on patients with hypertension and peripheral vascular disease confirm in general the findings of other authors.

Although the effects of C5 are greater and more prolonged than those of TEA, both drugs produce, after intravenous injection, an increase in skin temperature and to a lesser extent in skin resistance, but the results vary from day to day and, in patients with peripheral vascular disease, bear little relation to those to be expected from sympathectomy. The action on blood pressure in the normal subject is slight, though even small doses result in marked postural hypotension; the fall in blood pressure in hypertensive patients is roughly proportional to the degree of hypertension, and these patients also exhibit postural hypotension. There is an associated increase in heart rate. The action of C5 on the blood pressure can be correlated with that of amylobarbitone and with the response to the cold pressor test, but bears only an approximate relation to sympathectomy; the drug therefore may have its greatest value in hypertensive crises.

From their results the authors conclude that with increasing doses the drugs first produce tachycardia and postural hypotension, followed by a fall in blood pressure, vasodilatation, and inhibition of the galvanic reflex (the decrease in skin resistance following painful stimuli), and finally, with large doses, inhibition of the cold pressor response and an increase in skin resistance. Doses of 5 to 35 mg. C5 and 300 to 500 mg. TEA were given intravenously over several minutes.

C5 partially blocks the transmission of impulses across sympathetic, and possibly also parasympathetic, ganglia. Its failure to antagonize neostigmine shows that it does not compete with acetylcholine; it is, however, inhibited by adrenaline. It has no local action on blood vessels. TEA produces more widespread effects on all autonomic ganglia, on the neuromuscular junctions, and to some extent on the central nervous system and on sensory receptors; and it appears to compete with acetylcholine. *A. Paton*

51. **Hormones of the Sympathetic Nervous System and the Adrenal Medulla**
U. S. VON EULER. *British Medical Journal* [*Brit. med. J.*] **1**, 105–108, Jan. 20, 1951. 41 refs.

52. **The Role of Electrolyte Balance in the Response to Mercurial Diuretics in Congestive Heart Failure**
W. B. SCHWARTZ. *Bulletin of the New England Medical Center* [*Bull. New Engl. med. Center*] **12**, 213–218, Dec., 1950. 9 refs.

The refractory state to mercurial diuretics and its correction are discussed. Two factors are concerned—namely, reduction in glomerular filtration and changes in the serum electrolytes: the latter alone are considered. The serum electrolyte pattern may or may not change after diuresis, however produced. If the extra fluid passed in the urine contains electrolytes in the same proportion as in the extracellular body fluid, then the serum electrolyte levels do not alter. But if there is an excessive loss of chloride in the urine, then the chloride level in the serum falls. The converse is also true—if the chloride excretion in the urine is diminished, the chloride level in the serum rises.

After repeated injections of a mercurial diuretic the usual electrolyte change is as follows: in the urine there is an excessive loss of chloride, while in the serum the chloride level falls and the bicarbonate concentration

rises; the sodium content of the serum remains unchanged, but that of potassium may fall sharply; when the serum chloride level falls to 88 to 98 mEq. per litre (normal 102 to 106 mEq. per litre) and the serum bicarbonate content rises to 30 to 38 mEq. per litre (normal 25 to 29 mEq. per litre) the mercurial no longer causes a diuresis and the refractory state has developed. The administration of ammonium chloride is corrective because much of the chloride is retained and the chloride and bicarbonate levels in the serum become normal. Diuresis will follow the next injection of the mercurial, but if ammonium chloride is not continued, the refractory state will eventually return. It is clear, therefore, that ammonium chloride is essential in the treatment of many patients with mercurial diuretics. It should be remembered that ammonium chloride has a different action in subjects with a normal serum electrolyte pattern; in this case it causes a loss of chloride and sodium in the urine and consequently produces diuresis. The distinction between these two actions is, therefore, that when used as a corrective it restores the normal blood chemistry, subsequently allowing a mercurial to cause diuresis and possibly enhancing the action; when used where the blood chemistry is already normal, it is itself a diuretic.

Sometimes the refractory state does not develop, despite considerable changes in the serum levels of electrolytes. There is then a real danger of a metabolic catastrophe causing death in coma. This possibility should be considered when a patient's general condition deteriorates in spite of the relief of congestion. It can be detected by investigating the blood chemistry, and it can be prevented by administration of ammonium chloride.

Occasionally mercurials cause diuresis with no change in the electrolyte levels. This is unusual and unexplained, but fortunate because the refractory state does not develop. Sometimes the refractory state appears even though ammonium chloride is being given. This may be due to: (1) an initial great diuresis with excessive loss of chloride which is too large to be corrected by the usual dose of ammonium chloride; (2) inability to take the drug; (3) inability to dissolve the enteric-coated capsules. If the drug cannot be taken by mouth it can safely be given intravenously as a 1% solution in 5% glucose. The rate should not exceed 200 ml. in one hour (10 to 15 g. in 24 hours). If it is given more rapidly the liver is unable to convert the ammonia to urea and there is a danger of convulsions, coma, and death. Another remedy is to give dilute hydrochloric acid by mouth: the usual dose is 20 ml. of 10% hydrochloric acid in 24 hours, diluted in 600 to 1,000 ml. of water and given in divided doses. The syndrome of hypochloraemic alkalosis must be distinguished from the "low-salt" syndrome. In the former the serum chloride level is low, that of sodium normal, and of bicarbonate high. In the latter the serum chloride and sodium levels are low and there is an acidosis. The two can be differentiated by checking the blood chemistry. The low-salt syndrome is difficult to treat and has a poor prognosis. Hypertonic saline given intravenously may be helpful.

Arthur Willcox

53. **The Effect of Heparin on the Plasma Cholesterol**
D. P. BASU and C. P. STEWART. *Edinburgh Medical Journal* [*Edinb. med. J.*] **57**, 596–599, Dec., 1950. 6 refs.

In 19 patients the administration of 30,000 units of heparin during 24 hours was followed by a fall in the levels of both free and total cholesterol in the blood. The ratio of free to total cholesterol was not changed. In 5 patients with xanthomatosis or nephrotic syndrome the blood cholesterol level was high, and the fall (about 40%) was greater than in the remaining 11, who had coronary infarction and a normal blood cholesterol level, which fell about 20%. Further administration of heparin during the next 24 hours had no effect. Blood cholesterol levels returned to normal by the 5th day. The anticoagulant "tromexan" had no effect on blood cholesterol values.

V. J. Woolley

CHEMOTHERAPY

54. **The Action of Drugs *in vitro* on Cestodes: II. Non-anthelmintic Drugs.** [In English]
A. M. E. DUGUID and R. ST. A. HEATHCOTE. *Archives Internationales de Pharmacodynamies et de Thérapie* [*Arch. int. Pharmacodyn.*] **84**, 159–175, Dec., 1950. 15 figs., 9 refs.

The effects of more than 40 substances have been studied *in vitro* on the sheep tapeworm, *Moniezia expansa*. No evidence was obtained for the presence of cholinergic or adrenergic receptors in this cestode, but cholinesterase and amine oxidase may be present. Strong solutions of emetine and cephalin produced an irreversible change in the worm's smooth muscle, resembling rigor mortis in skeletal muscle. Morphine increased tone and movement of the worm, but codeine and thebaine were depressant in action. Coniine, structurally related to pelletierine, had a powerful, but reversible, depressant effect on movement. None of the compounds tested is likely to be clinically useful. The results are not all in agreement with those obtained by Baldwin on *Ascaris*, the difference presumably being due to the use of different species by the two groups of workers.

Derek R. Wood

55. **The Reactions of Bacteria to Chemotherapeutic Agents**
L. P. GARROD. *British Medical Journal* [*Brit. med. J.*] **1**, 205–210, Feb. 3, 1951. 4 figs., bibliography.

ANTIBIOTICS

56. **The Effect of Combinations of Antibiotics on Enterococci *in vitro***
J. B. GUNNISON, E. JAWETZ, and V. R. COLEMAN. *Journal of Laboratory and Clinical Medicine* [*J. Lab. clin. Med.*] **36**, 900–911, Dec., 1950. 5 figs., 24 refs.

Clinical experience has suggested that infections of the urinary tract and of the endocardium due to enterococci, which are usually resistant to treatment with penicillin or streptomycin, may be controlled by aureomycin or by streptomycin and penicillin in combination. In the

present work the bacteriostatic and bactericidal action on large populations of enterococci of penicillin, streptomycin, aureomycin, and chloramphenicol, singly and in various combinations, was studied *in vitro*. The strains used had recently been isolated from the blood of patients with subacute endocarditis or from the urine in cases of urinary-tract infection. The effects of single antibiotics were recorded in terms of " static concentration " (the minimum initial concentration preventing visible growth for 4 days) and of " lethal concentration " (minimum initial concentration killing more than 99·99% of organisms within 28 days); for penicillin the " optimum concentration " (the initial concentration producing the highest rate of death in 48 hours) was also recorded.

With penicillin optimum bactericidal concentrations against 10 strains of enterococcus varied from 6 to 30 μg. per ml. Higher concentrations gave lower bactericidal rates, but usually sterilized the medium within 10 days. With streptomycin alone the static concentration ranged from 250 to 1,000 μg. per ml., and chloramphenicol alone caused only a slight reduction in multiplication at concentrations up to 50 μg. per ml. Aureomycin had a definite early bactericidal effect, but failed to sterilize the cultures even at concentrations as high as 500 μg. per ml. Streptomycin enhanced both the bactericidal and bacteriostatic effects of penicillin, reducing the lethal concentration by 95%, while chloramphenicol slightly enhanced its bacteriostatic and ultimate bactericidal properties. Aureomycin, however, was antagonistic to penicillin in tests extending over 48 hours. A combination of penicillin, aureomycin, and streptomycin was more effective than any of these drugs alone or in pairs, the lethal concentration of penicillin being reduced by as much as 98%; when chloramphenicol was substituted for aureomycin the combination was rather less effective than penicillin paired with streptomycin, but superior to penicillin alone. The joint effect of all four drugs given simultaneously was greater than that of any two or three in combination, with the exception that bactericidal rates were slower than with penicillin plus streptomycin.

The total effect of mixtures of three or four antibiotics thus tested appears to be the resultant of the antagonistic and synergistic effects of the participating pairs. The experimental demonstration of anatagonism between antibiotics *in vitro* makes the indiscriminate use of combinations of antibiotics in clinical practice inadvisable. *J. F. McCrea*

57. The Therapy of Experimental Psittacosis and Lymphogranuloma Venereum (Inguinale). I. The Comparative Efficacy of Penicillin, Chloramphenicol, Aureomycin, and Terramycin

E. Weston Hurst, J. M. Peters, and P. Melvin. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 611–624, Dec., 1950. 9 refs.

The virus strains used were: (1) A lymphogranuloma venereum virus (LGV) maintained by passage through developing hens' eggs. This virus was passed intracerebrally and intraperitoneally in mice, and a virus obtained which infected mice on intraperitoneal injection. LGV infections were treated both in egg yolk and in mice. (2) The M.O.H.154 strain of psittacosis virus maintained by intraperitoneal injection in mice. (3) K.L.G. virus, supposed to be a mouse-virulent lymphogranuloma venereum virus, but immunologically being more nearly related to psittacosis virus: it was maintained as for (2).

The yolk sacs of groups of about 20 6-day embryos were infected with LGV virus, and 2 hours later one of the test substances or water was injected. Untreated controls died in about 4 days. With treatment longer survival occurred, and some survived until the 20th day of incubation, when the eggs were opened. Terramycin was most effective; 0·1 mg. increased mean survival time of one group to 11·2 days. The other antibiotics were less effective in the order aureomycin, chloramphenicol (in propylene glycol), and penicillin.

The tests on mice were severe; 10^3 or $10^5 \times$ LD50 was injected intraperitoneally into groups of 30 mice, and treatment was sometimes delayed for several days. The authors stress the importance of observing animals for a long period after treatment stops. In one group treated for 12 days with chloramphenicol only 6 mice died before the 21st day, but 18 died between the 22nd and 39th days. The average survival of controls was 6·7 days.

The different strains showed similar responses to treatment. Aureomycin and terramycin were most effective; doses of 1 or 2 mg. orally twice daily for 12 days often reduced the number of deaths from about 25 out of 30 to 0 or 1 out of 30. Procaine penicillin, 30,000 units per 20 g. body weight subcutaneously every third day, was also effective. Chloramphenicol was less effective. A combination of aureomycin with procaine penicillin was not more effective than aureomycin alone. Aureomycin (oral) was effective against virus introduced intracerebrally, intravenously, or intraperitoneally, while penicillin given subcutaneously was effective only against intraperitoneal virus.

The amount of virus in 6 pooled spleens was titrated in other mice on each of the first 6 days of treatment. The results confirmed the effectiveness of the antibiotics in suppressing the virus—aureomycin, for example, reducing the amount of virus by a factor of about 10^6. The persistence of virus in the spleens of mice surviving infection was shown when pooled spleens were passed into test mice. When 10% suspensions of individual spleens were passed into 3 mice, virus was detected in 50% of the spleens of control survivors. The percentage of carriers in treated mice varied. The earlier treatment started, the greater the percentage of carriers. Those treated with penicillin only showed 24% carriers among the survivors; aureomycin treatment, however, left 65·3% carriers. The evidence suggests that this difference was not merely due to the fact that a large number of animals survived after aureomycin, since the proportion of the total number of mice infected which appeared as carriers was less with penicillin than with aureomycin. The large number of carriers among the aureomycin-treated mice at 35 to 50 days contrasted with the comparative paucity of virus during treatment and suggested that the virus grew again after treatment stopped. A direct experiment confirmed this; half of a group of mice surviving after aureomycin for 12 days were killed on the 13th day, the remainder were killed

on the 40th day. The spleens of the latter group contained more virus than the spleens of the former.

R. P. Stephenson

58. **" Benemid " *p*-(Di-n-propylsulfamyl)-benzoic Acid: Lack of Effect of Aureomycin, Chloromycetin, Streptomycin and Terramycin**
W. P. Boger, W. V. Matteucci, and J. O. Beatty. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **76**, 222–225, Feb., 1951. 2 figs., 13 refs.

59. **Enhancement of the Action of Streptomycin**
R. J. W. Rees and J. M. Robson. *Science* [*Science*] **112**, 790–791, Dec. 29, 1950. 3 figs., 9 refs.

The authors describe the experimental treatment of tuberculous lesions of the cornea in rabbits and mice with combinations of streptomycin and various other drugs, the results of which confirm the statement of Woody and Avery (*Science*, 1948, **108**, 501), that the action of streptomycin against the tubercle bacillus can be enhanced by combining it with potassium iodide. They found that this enhancement was more definite in advanced caseous tuberculosis than in very early lesions. Their findings also confirm the work of Bavin (*J. Pharm. Pharmacol.*, 1949, **1**, 790), who showed that the effect of *p*-aminosalicylic acid (2% in the diet) was not enhanced by the addition of potassium iodide. They report that treatment either with streptomycin alone or with *p*-aminosalicylic acid alone was more effective than treatment with a streptomycin *p*-aminosalicylate compound.

A. W. H. Foxell

60. **Biological Activity of Combinations of Streptomycin and Fatty Acids.** (Activité biologique des combinaisons streptomycine–acides gras)
F. Gros, M. Machebœuf, M. Beljanski, F. Grumbach, and F. Boyer. *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences* [*C.R. Acad. Sci., Paris*] **232**, 764–766, Feb. 19, 1951. 4 refs.

Streptomycin can form compounds with fatty acids, usnic acid, heparin, and phospholipids. A compound, termed oleostreptomycin, is formed by mixing 10 ml. of 10% solution of streptomycin sulphate with 22 ml. of 2% solution of sodium oleate. A precipitate is formed and washed with water. It decomposes at 160° to 170° C. and is soluble in propylene glycol. The combination yields a product containing 4 molecules of oleic acid to one molecule of streptomycin.

The effects of equimolar solutions of dihydrostreptomycin sulphate and oleostreptomycin were compared *in vitro* on the growth of *Staphylococcus aureus*, *Bacterium coli*, and *Diplococcus pneumoniae*. The inhibitory power of oleostreptomycin was 20% greater than that of dihydrostreptomycin. For *Mycobacterium tuberculosis*, in Youmans's or Dubos's media, the inhibitory power of the two compounds was equal. The acute toxicity of oleostreptomycin in mice was such that a dose equivalent to 2,000 μg. of streptomycin per g. caused no mortality, although all mice were killed in 4 hours with half this dose of dihydrosteptomycin. Six injections of oleostreptomycin, each equivalent to 1,600 μg. of streptomycin per g. body weight, on 6 successive days caused no mortality. In mice, treatment with oleostreptomycin and treatment with dihydrostreptomycin in daily doses equivalent to 1 mg. of streptomycin base per animal were equally effective. With *Diplococcus pneumoniae* in mice the two compounds also were equally active. Combinations of streptomycin with hydnocarpic acid, undecylenic acid, and *iso*linoleic acid have also been produced.

G. M. Findlay

61. **Synergism in the Anti-tuberculous Therapeutic Activity between β-Pyridine-aldehyde-thiosemicarbazone (" G. 469 ") and Dihydrostreptomycin.** (Synergie de l'activité thérapeutique antituberculeuse de l'association entre la β-pyridine-aldéhyde-thiosemicarbazone (G 469) et la dihydrostreptomycine)
C. Levaditi, A. Girard, A. Vaisman, A. Ray, and H. Chaigneau-Erhard. *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences* [*C.R. Acad. Sci., Paris*] **232**, 770–772, Feb. 19, 1951. 3 refs.

In mice infected with tuberculosis " G 469 " is said to have an activity equal to that of thiacetazone. Experiments were carried out to determine whether G 469 and dihydrostreptomycin have a synergistic action. A daily dose of 500 units of dihydrostreptomycin for 27 days (total 13,500 units) per 20 g. body weight was the minimum curative dose. G 469 in a daily dose of 0·5 mg. per 20 g. body weight caused a 50% mortality. However, with a daily dose of 500 units of dihydrostreptomycin and 0·5 g. G 469 per 20 g. there was no death, and the lesions showed healing similar to that provided by daily doses of dihydrostreptomycin alone of 1,000 to 2,000 units per 20 g.

G. M. Findlay

62. **Panmyelophthisis following Streptomycin Therapy** (Panmyelophthise unter Streptomycin-Behandlung)
U. Gaede and K. Palm. *Tuberkulosearzt* [*Tuberkulosearzt*] **5**, 26–30, Jan., 1951.

Toxic reactions of the haematopoietic system after streptomycin treatment have already been reported in the literature. In this paper an unusual, fatal, case of allergic reaction to streptomycin is described in a woman of 44 who had suffered from pulmonary tuberculosis for 18 years. Her mother and brother had died from tuberculosis, and her father suffered from pernicious anaemia. The patient's condition had been exacerbated 11 years. previously after cutaneous tuberculinization (? provoked allergy). Two years later she had had a course of gold injections, apparently without undue reaction. In January, 1949, she developed an acute bilateral pleural effusion (? allergic) which was resorbed within 8 weeks. In July, 1949, a course of thiacetazone was started, but was discontinued after a total of 1·05 g. had been given because of pyrexia and spread of infection, whereupon she improved and her temperature returned to normal. Ten days after the termination of thiacetazone treatment a course of streptomycin in doses of 0·25 g. twice a day was started, with gradual improvement subjectively and also radiologically. After 2 months, and a total dosage of 30g., the patient complained of slight drowsiness, which

gradually subsided, and later had an attack of migraine lasting some hours. At the beginning of January, 1950, there was sudden onset of purpura haemorrhagica, the streptomycin having been discontinued the previous day because of slight dizziness after a total dose of 58·75 g. had been given. The haemoglobin level was 56%, erythrocyte count 3,000,000 per c.mm., leucocytes 1,900 per c.mm., and thrombocytes 55,000 per c.mm. Bleeding time was 11¼ minutes and clotting time 4½ minutes. There was menorrhagia and subfebrile temperature. In spite of vigorous treatment with blood transfusions and vitamins, the blood picture deteriorated and at the time of death the haemoglobin level was 30%, erythrocyte count 1,900,000 per c.mm. and leucocyte count 320 per c.mm., mostly lymphocytes. The thrombocytes numbered 8,000 per c.mm. and clotting time was 15 minutes. No necropsy was performed, but puncture of the spleen, tibia, and iliac crest was carried out post mortem and yielded scanty lymphocytes only. Blood examination during and after treatment with thiacetazone showed no abnormality. The acute destruction of the haematopoietic apparatus is interpreted as due to allergic shock.

[Among the lessons to be learnt from this case is that streptomycin should not be given indiscriminately, as it so often is nowadays. A history of allergic reactions to other drugs should be regarded as a warning signal and streptomycin must be discontinued as soon as side-effects such as dizziness, drowsiness, or migraine are noted. The patient must be warned to report any such symptoms at once.] *E. G. W. Hoffstaedt*

63. **Ineffectiveness of Aureomycin in Preventing the Primary Vaccinia Reaction**
R. H. High and C. B. Reiner. *Journal of Pediatrics* [*J. Pediat.*] **38**, 60–62, Jan., 1951. 8 refs.

The evolution of the primary vaccinia reaction is not affected by the concurrent administration of aureomycin in doses of approximately 50 mg. per kilo. per day for a period of 5 days.—[Authors' summary.]

64. **Bacteriological Control of Aureomycin Therapy**
E. Topley, E. J. L. Lowbury, and L. Hurst. *Lancet* [*Lancet*] **1**, 87–89, Jan. 13, 1951. 3 figs., 5 refs.

65. **Studies on the Administration, Absorption, Distribution and Excretion of Aureomycin in Children. With Observations Concerning Tolerance, Dosage Schedules and Certain Therapeutic Indications**
C. M. Whitlock, A. D. Hunt, and S. G. Tashman. *Pediatrics* [*Pediatrics*] **6**, 827–842, Dec., 1950. 4 figs., 28 refs.

This paper records observations on the administration, absorption, distribution, and excretion of aureomycin in 150 patients, ranging from newborn infants to adults. The authors' conclusions may be summarized as follows.

Aureomycin in doses of approximately 11 mg. per kg. body weight given orally at 4-hour intervals is well-tolerated by the majority of infants and children. Satisfactory serum levels are obtained with this dosage. Single doses larger than 11 mg. per kg. body weight do not produce significantly higher serum levels. The incidence of vomiting among 48 children on such a dosage schedule was 19% (9 cases). Gastro-intestinal tolerance was increased when aluminium hydroxide gel or 3 to 4 oz. (85 to 114 ml.) of milk was given following each dose. When the intravenous route is employed the recommended dosage is 6·6 mg. per kg. body weight every 12 hours. The intramuscular route is unsatisfactory as it causes intense local pain and frequent febrile reactions. Rectal administration was tried in 3 cases but was found to be unreliable and often painful.

The peak serum level is reached somewhere between one and 4 hours after ingestion. This level is low but is maintained until 6 to 8 hours after ingestion. On the other hand, after intravenous administration there is a rapid rise and fall of the aureomycin level in the serum. The authors suggest that aureomycin is distributed rather uniformly throughout the body, but that it does not enter the erythrocytes. The fact that carinamide does not seem to affect the slope of the serum aureomycin level curve suggests that tubular excretion plays a negligible role, and that renal excretion is glomerular alone. *A. W. H. Foxell*

66. **The Action *in vitro* of Aureomycin on Various Strains of Brucellae and Salmonellae.** (Sull'azione *in vitro* dell'aureomicina su diversi ceppi di Brucelle e di Salmonelle)
F. Scanga. *Rendiconti Istituto Superiore di Sanita* [*R.C. Ist. sup. San.*] **13**, 534–545, 1950. 27 figs., 33 refs.

A total of 27 strains of *Salmonella* and *Brucella* were tested *in vitro* for sensitivity to aureomycin by the author's modification of the standard technique. Agar plates were seeded with either 0·1 or 1 ml. of a 24- to 48-hour culture of organisms per 20 ml. of agar. Four depressions on each plate were then filled with 0·1, 1, 10, and 100 μg. of aureomycin and the plates incubated, for 24 hours in the case of salmonellae and 48 hours in the case of brucellae.

On exposure to 0·1 μg. of antibiotic, a strain of paratyphoid A was the only salmonella significantly inhibited, while only one strain of brucellae was resistant. With 1 μg., however, 5 of the 13 salmonella strains and all of the brucellae were significantly inhibited. Only one salmonella strain remained resistant to 100 μg. The most sensitive salmonella was *Salm. paratyphi* A, the least sensitive *Salm. typhi*; the most sensitive brucella was *Br. suis*, and the least sensitive *Br. melitensis*. The possible clinical bearing of these varying sensitivities is briefly discussed, and it is pointed out that the effective therapeutic concentration in serum would have to be at least 5 times higher than that found *in vitro*.

Electron micrographs were made of a strain each of *Salm. typhi*, *Bacterium coli*, and *Br. melitensis*. With *Salm. typhi* the protoplasm becomes granular, and at high concentrations of aureomycin may contract into the centre of the bacterial body. *Bact. coli* and *Br. melitensis* behave similarly in that the bacteria swell markedly and then divide abnormally, giving rise to coccoid forms. In some instances lysis occurs as the final stage.

[The electron micrographs illustrating this paper are exceptionally fine.] *J. F. McCrea*

67 (*a*). **Bacterial Variants in Patients Treated with Chloramphenicol**
A. VOUREKA. *Lancet* [*Lancet*] **1**, 27–28, Jan. 6, 1951. 1 fig.

67 (*b*). **Production of Bacterial Variants *in vitro* with Chloramphenicol and Specific Antiserum**
A. VOUREKA. *Lancet* [*Lancet*] **1**, 28–31, Jan. 6, 1951. 3 figs., 3 refs.

In the first of these two papers the author describes the appearance of atypical bacterial colonies of *Pseudomonas aeruginosa* or *Bacterium coli* which developed in cultures of the urine of several patients under treatment with chloramphenicol. After a few days' treatment the urine became sterile, but if the drug was continued colonies again appeared on plating. These colonies showed profound morphological and cultural changes, but reverted to the original type after several subcultures.

In the second paper the author describes experiments performed with *Bact. coli* as the test organism. Cultivation in broth plus chloramphenicol produced distorted organisms which, on plating, yielded normal colonies. When a specific antiserum was added to the culture, changes occurred in both the colonial and cellular morphology of the bacteria. Subculture on solid media yielded scanty growths of three new types of colony. Two of these reverted to the original type after a varying number of subcultures, but the third has been replated some 200 times without any such reversion. The variants were shown to have lost their virulence for mice and 2 of them to have lost the ability to ferment certain sugars. They showed altered resistance to penicillin, potassium tellurite, and streptomycin, resistance in some cases being higher, in others lower, than that of the original strain. All the variants except one were either equally or more sensitive to chloramphenicol compared with the original strain.

The author believes these changes to be due to a true mutation, but not necessarily the result of a specific action of chloramphenicol. The production of such variants might be brought about by any agent causing the cell an injury. *A. W. H. Foxell*

68. **Experimental Study *in vitro* on the Action of Chloramphenicol on the Viruses of Vaccinia, Foot-and-mouth Disease, and Rabies.** (Ricerche sperimentali *in vitro* sull'azione della cloromicetina nei confronti del virus vaiolo vaccino, del virus aftoso, e del virus rabido fisso)
L. RAVAIOLI and R. NEGRI. *Rendiconti Istituto Superiore di Sanita* [*R.C. Ist. sup. San.*] **13**, 546–554, 1950. 5 refs.

Serial dilutions of vaccinia, rabies, and foot-and-mouth disease viruses were exposed to doses of chloramphenicol ranging from 1 μg. to 1 mg. for 5 hours. The activity of vaccinia virus was not affected as judged by the number of pustules produced on scarified rabbit skin, nor was the infectivity or rate of multiplication of foot-and-mouth disease virus reduced. Concentrated suspensions of rabies virus were still fully infective for rabbits on intracerebral injection, but the highest dilution (approximately 10 μg. of virus) was inactivated after exposure to 100 μg. of chloramphenicol per ml. *J. F. McCrea*

69. **Toxic Effects of Chloramphenicol.** (Sur les accidents de la chloromycétine)
Y. BOQUIEN, D. HERVOUET, —. DAUPHIN, and —. VERDIER. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **66**, 1493–1501, Nov. 17, 1950.

Toxic effects of varying severity were observed in 22 out of 180 cases of typhoid and paratyphoid fevers treated with chloramphenicol. These were of two main types: delayed collapse and digestive disturbances. Delayed collapse, occurring on the second to third day of treatment, was observed in 3 cases. The temperature fell to 36° or 35° C., and bradycardia (40 per minute) and prostration appeared. This state persisted for several days following the cessation of chloramphenicol, after which recovery occurred. Digestive disturbances usually appeared on the third day of treatment and took one of three forms. The first consisted of nausea, vomiting, severe diarrhoea, and dehydration; there was no abdominal pain or meteorism and no fall in blood pressure; three of these cases were fatal. In the second form the above symptoms were associated with a fall in temperature and a rising pulse rate. Recovery occurred in 2 cases after the treatment had been stopped at the first appearance of symptoms. The third form, which occurred in 17 cases, consisted of mild vomiting or diarrhoea and responded to reduction of dosage or cessation of choramphenicol. *I. Ansell*

70. **Synnematin, an Antibiotic Produced by *Tilachlidium***
R. Y. GOTTSHALL, J. M. ROBERTS, L. M. PORTWOOD, and J. C. JENNINGS. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **76**, 308–311, Feb., 1951. 3 refs.

71. **Observation on Absorption of Bacitracin. Blood Levels following All Administration**
A. B. LONGACRE and R. M. WATERS. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **92**, 213–216, Feb., 1951. 6 refs.

72. **Fungicidin, an Antibiotic Produced by a Soil Actinomycete**
E. L. HAZEN and R. BROWN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **76**, 93–97, Jan., 1951. 3 figs., 8 refs.

Fungicidin is an antibiotic obtained from a soil actinomycete belonging to the genus *Streptomyces*: the species has not yet been determined. The isolation and chemical and physical properties of fungicidin are described. It was found *in vitro* to have fungistatic and fungicidal activity against a wide variety of saprophytes and pathogenic forms in concentrations ranging from 1·56 to 6·25 μg. per ml. Its activity was not diminished by the presence of horse blood or serum. Tests *in vivo* were carried out on white mice of 20 to 25 g.

The LD50 for crude fungicidin if administered intraperitoneally was between 20 and 26 mg. per kg. body weight. Injected subcutaneously, a dose of 2 g. per kg. was not lethal. Therapeutically, it appeared to be of value in histoplasmosis and cryptococcosis induced in mice.

A. W. H. Foxell

73. **Papers on Viomycin.** *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **63**, 1–48, Jan., 1951.

(*a*) **Viomycin: a New Antibiotic Active against Mycobacteria**
A. C. FINLAY, G. L. HOBBY, F. HOCHSTEIN, T. M. LEES, T. F. LENERT, J. A. MEANS, S. Y. P'AN, P. P. REGNA, J. B. ROUTIEN, B. A. SOBIN, K. B. TATE, and J. H. KANE. 5 refs.

(*b*) **Viomycin, a New Tuberculostatic Antibiotic**
Q. R. BARTZ, J. EHRLICH, J. D. MOLD, M. A. PENNER, and R. M. SMITH. 1 fig., 1 ref.

(*c*) **Antimicrobial Activity of *Streptomyces floridae* and of Viomycin**
J. EHRLICH, R. M. SMITH, M. A. PENNER, L. E. ANDERSON, and A. C. BRATTON. 1 ref.

(*d*) **The Activity of Viomycin against *Mycobacterium tuberculosis* and Other Microorganisms *in vitro* and *in vivo***
G. L. HOBBY, T. F. LENERT, M. DONIKIAN, and D. PIKULA. 12 refs.

(*e*) **The Effect of Viomycin *in vitro* and *in vivo* on *Mycobacterium tuberculosis***
C. P. YOUMANS and A. S. YOUMANS. 12 refs.

(*f*) **Viomycin in Experimental Tuberculosis**
W. STEENKEN and E. WOLINSKY. 1 fig., 5 refs.

(*g*) **The Effect of Viomycin in Tuberculosis of Guinea-Pigs, including *in vitro* Effects against Tubercle Bacilli Resistant to Certain Drugs**
A. G. KARLSON and J. H. GAINER. 2 figs., 6 refs.

(*h*) **Viomycin. Acute and Chronic Toxicity in Experimental Animals**
S. Y. P'AN, T. V. HALLEY, J. C. REILLY, and A. M. PEKICH. 1 fig., 3 refs.

Viomycin is an antibiotic derived independently by two groups of workers from *Streptomyces puniceus* and *Streptomyces floridae*. It is not yet known whether these two strains of streptomycete are identical. Viomycin is a strong organic base, and it forms neutral salts of which the sulphate, oxalate, and hydrochloride have been prepared in crystalline form. Its importance lies in the fact that while it shows moderate activity against various organisms, including coliform organisms, the meningococcus, and the diphtheria bacillus, it is relatively more active against the mycobacteria than other species. All the workers in a number of centres whose reports are collected here agree that it is equally active against streptomycin-sensitive and streptomycin-resistant strains of the tubercle bacillus and inhibits them in concentrations of 0·78 to 12·5 μg. of viomycin per ml. Its inhibitory effect is not antagonized by the presence of serum and tends to increase with increasing initial *p*H in the range between 7·1 and 8·5. Hobby *et al.* state that viomycin has a synergistic tuberculostatic effect when combined with streptomycin, but Karlson and Gainer deny this. Viomycin-resistant strains of tubercle bacilli can be produced *in vitro* after 5 or 6 transfers in " tween "-albumin liquid medium. In this way organisms resistant to 250 μg. of viomycin per ml. can be obtained. It is probable that viomycin-resistance develops more slowly than streptomycin-resistance.

Experiments *in vivo* are reported on mice and guinea-pigs infected with virulent strains of tubercle bacilli. Complete protection was afforded to mice for 23 days on a dosage of 1·5 to 8·0 mg. of viomycin sulphate per day. It is estimated that 40 mg. of viomycin a day affords as much protection to guinea-pigs as 10 mg. of streptomycin per day. Doses of 70 to 140 mg. per kg. body weight per day, while protecting guinea-pigs from dissemination of tuberculosis, will not eradicate a tuberculous abscess at the site of inoculation. Hobby *et al.* state that the acute intravenous LD50 for a 20-g. mouse is approximately 165 mg. of the pure base per kg. body weight, but P'an *et al.* find that it is 241 mg. per kg. body weight for an 18- to 22-g. mouse. The subcutaneous LD50 is 1,381 mg. per kg. body weight. Oral toxicity is very low. As regards chronic toxicity, Youmans and Youmans attribute the death of 27 mice to viomycin, but when a less toxic compound became available, doses of 12 mg. a day were tolerated for 28 days. Whereas rats and dogs tolerated 50 to 100 mg. per kg. body weight daily for several weeks without ill effect, cats showed disturbances of posture and gait after 4 to 7 weeks on this dosage. It is not yet known whether these changes are reversible if the drug is stopped.

A. W. H. Foxell

74. **The Toxicity of Viomycin in Humans**
C. A. WERNER, R. TOMPSETT, C. MUSCHENHEIM, and W. MCDERMOTT. *American Review of Tuberculosis* [*Amer. Rev. Tuberc.*] **63**, 49–61, Jan., 1951. 8 refs.

This paper describes the toxic effects encountered during the treatment with viomycin (see Abstract 73) of 10 patients with advanced chronic pulmonary tuberculosis, all but two of whom had previously received streptomycin, with or without other forms of treatment. The dosage employed was 30 to 75 mg. of the hydrochloride or sulphate per kg. body weight for 14 to 182 days, injected intramuscularly at 6- or 12-hourly intervals. The initial sensitivity of the organisms lay within the range 6·2 to 12·5 μg. of viomycin per ml. of medium. A 2- to 16-fold increase in resistance was seen, but an 8- to 16-fold increase did not occur with less than 62 days' treatment.

The 3 patients who were treated with the hydrochloride developed painful, fluctuant nodules at the site of injection, but no local reaction occurred when the sulphate was substituted. Two patients developed eosinophilia, with urticaria or a pruritic erythema. Nine patients developed albuminuria, with casts, erythrocytes, and leucocytes in the urine; in 4 the blood urea level was raised, the highest figure being 35 mg. per 100 ml. Five patients complained of anorexia, nausea,

lassitude, muscle cramps, and paraesthesiae, which were associated with a reduced serum content of potassium, calcium, phosphorus, and chlorides and a raised carbon dioxide combining power; these abnormalities necessitated discontinuance of the drug in 4 cases, and intensive replacement therapy with potassium and calcium salts; they can be explained only partially by the toxic action of viomycin on the kidneys. Two patients developed impairment of vestibular function and partial deafness. No changes were seen in the blood. All these signs of toxicity were reversible, and disappeared when administration of viomycin was stopped.

The disease in these cases was too far advanced for a definite therapeutic evaluation to be made from them. It is, however, encouraging to note that slight to moderate improvement was recorded in 5 cases. The toxicity encountered was not sufficiently severe to discourage further clinical trial on a more suitable group of patients.

A. W. H. Foxell

75. **Neomycin: Results of Clinical Use in Ten Cases**
G. G. DUNCAN, C. F. CLANCY, J. R. WOLGAMOT, and B. BEIDLEMAN. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **145**, 75–80, Jan. 13, 1951. 1 fig., 4 refs.

Neomycin is a new antibiotic obtained from *Streptomyces fradiae*. The authors have tested it in 6 cases of pyelonephritis and 4 cases of cystitis, some with complications such as bacteriaemia, at the Pennsylvania Hospital, Philadelphia. The causative organisms included *Aerobacter aerogenes*, *Bacterium coli*, paracolon bacilli, *Pseudomonas aeruginosa*, non-haemolytic streptococci, haemolytic staphylococci, and *Proteus*. All these organisms were shown to be completely or partially resistant *in vitro* to penicillin, aureomycin, chloramphenicol, and streptomycin, but in all but one case were sensitive to neomycin (200 units per ml.). Only in the case from which the resistant organism was isolated did the patient fail to improve on treatment, bacteriological evidence of cure being obtained in all the others. Serum and urine assays of the drug were carried out at frequent intervals. Sulphobromophthalein sodium retention tests, phenolsulphonphthalein excretion tests, electrocardiography, blood and bone-marrow examinations, retinoscopy, audiography, blood urea nitrogen estimations, and urine examinations were carried out before and after treatment and showed evidence of toxicity in only one case. This patient had a persistent elevation of the blood urea nitrogen level, with transient nausea and vomiting and transient impairment of hearing as shown by the audiogram. Dosage varied from 4,498 units (for an infant) to 100,000 units every 6 hours for 4 doses, followed by 50,000 to 100,000 units every 12 hours for 5 to 7 days. In the blood a stable level of 4 to 10 units per ml. was reached in 48 to 72 hours. Maximum urinary levels varied from 26 to 410 units per ml. No relapse has been recorded, the follow-up period ranging from 1 to 4 months. Most strains of *Proteus* and, more especially, of *Pseudomonas* exhibited properties suggesting the potential development of resistance to neomycin.

J. Maclean Smith

76. **Antibiotic Action of a Fungus from the Soil of a Truffle Ground.** (Pouvoir antibiotique d'un champignon provenant d'une terre de truffière)
R. DUJARRIC DE LA RIVIÈRE and P. R. BRYGOO. *Comptes Rendus Hebdomadaires des Séances de l'Académie des Sciences* [*C.R. Acad. Sci., Paris*] **232**, 454–455, Jan. 29, 1951. 1 ref.

A fungus which appears to be intermediate between *Mortierella alpina* Peyronel and *Mort. renispora* Stewart has been isolated from the soil of a truffle ground. The fungus grows on gelatin or in broth under aerobic conditions: it grows at +4° C. or at room temperature. A diffusible antibiotic is produced, which appears after 4 or 5 days' growth and increases up to the 9th day. The antibiotic is active *in vitro* against streptococci, gonococci, staphylococci, and pneumococci in decreasing order. It has hardly any action on *Proteus* or *Bacterium coli*. The action is bacteriostatic.

Neither *Mort. pusilla* var. *isabellina* nor *Mort. bainieri* produces an antibiotic, and Wilkins and Harris (*Brit. J. exp. Path.*, 1943, **24**, 141) failed to find any antibiotic in *Mort. reticulata*.

G. M. Findlay

77. **On Antibiotic Effects of Lichens and Lichen Substances.** [In English]
K. O. VARTIA. *Annales Medicinae Experimentalis et Biologiae Fenniae* [*Ann. Med. exp. Biol. fenn.*] Suppl. 7, **28**, 1–82, 1950. 13 figs., bibliography.

TOXICOLOGY

78. **Chronic Poisoning due to Excess of Vitamin A. Description of the Clinical and Roentgen Manifestations in Seven Infants and Young Children**
J. CAFFEY. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 12–26, Jan., 1951. 9 figs., 10 refs.

The cases are described of 7 patients who had been given excessive doses of concentrates of vitamins A and D over a period of several months without the knowledge of their medical attendants. In all cases the daily dosage of vitamin A exceeded 75,000 units. There was a latent period of at least 6 months before this produced symptoms. In each case the blood vitamin-A level was high and the patient improved rapidly after administration was stopped.

The principal clinical features were irritability, limitation of movement, and tender swellings attached to bones. In several cases there was a rather vague history of premonitory anorexia and pruritus for weeks or months before the onset of major symptoms. Radiologically, subperiosteal hyperostosis was found underlying the tender swellings. Both ulnae and one or more metatarsals were found to show such hyperostosis in each of the cases examined. Other bones affected included the clavicles, radii, metacarpals, lower ribs, femora, tibiae, and fibulae.

In the past the condition of hypervitaminosis A has been confused with infantile cortical hyperostosis. This latter condition, however, appears during the first 4

months of life, whereas hypervitaminosis A has never been recorded before the 12th month. In cases of infantile cortical hyperostosis there are always swelling of the face and jaws and thickening of the mandible; involvement of these structures has never been seen in hypervitaminosis A. These and other differences should serve to distinguish the two conditions in future.

J. A. Shiers

79. **Acute Phosphorus Poisoning in Man: a Study of 56 Cases**

R. S. Díaz-Rivera, P. J. Collazo, E. R. Pons, and M. V. Torregrosa. *Medicine* [*Medicine, Baltimore*] **29**, 269–298, Dec., 1950. 40 refs.

Poisoning by yellow phosphorus has virtually disappeared in Britain with the introduction of less dangerous rodenticides. Puerto-Ricans, on the contrary, find it a cheap and useful suicidal agent; no fewer than 56 cases were admitted to one hospital in San Juan in a recent 3½-year period, 27 deaths ensuing. The only significanct factors were the patient's age, the amount taken, and the vehicle, about 1 g. constituting a minimum lethal threshold, and a fluid vehicle (especially if alcoholic) increasing the mortality. Early vomiting or a washout within the first 5 hours much improved the prognosis.

Of the 56 patients 41 developed hepatomegaly, a dangerous early sign, within 24 hours; both this and early jaundice were directly related to the quantity of phosphorus absorbed. Circulatory collapse, haemoconcentration, oliguria, delirium, toxic psychoses, and azotaemia (developing in two-thirds of the cases) also occurred. The majority of deaths took place before the Hangar (cephalin–cholesterol) flocculation reaction became positive; liver function tests proved of little use. Hyperphosphataemia was noted in 8 cases without a fall in serum calcium level, indicating "tissue fixation of absorbed phosphorus". BAL was given to 24 patients "with poor results"; a routine 1 : 1,000 potassium permanganate washout, together with the administration of mineral oil, was the most effective treatment. Early deaths, up to 48 hours, were from circulatory collapse ascribed to direct myocardial damage: later deaths, mostly within a week, were from a hepatorenal syndrome with jaundice and azotaemia. *Keith Simpson*

80. **The Isolation of a Toxic Substance from Agenized Wheat Flour**

P. N. Campbell, T. S. Work, and E. Mellanby. *Biochemical Journal* [*Biochem. J.*] **48**, 106–113, Jan., 1951. 2 figs., 27 refs.

Mellanby (*Brit. Med. J.*, 1946, **2**, 885) showed that feeding of agenized flour to dogs resulted in the production of "running fits". The present authors describe the isolation of a toxic substance from agenized flour which is probably identical with that isolated from agenized zein by Bentley *et al.* (*Nature, Lond.*, 1949, **164**, 438). The method consisted in the digestion of the separated gluten with pepsin and trypsin, dialysis against distilled water, acid hydrolysis, electrodialysis, removal with charcoal of the aromatic amino-acids, fractionation on a "zeo-karb" column, and finally fractionation on a paper column. The toxic substance was then obtained in a crystalline form. All stages were controlled by toxicity tests with ferrets. The final product was toxic in a dose of 3 mg. fed over 5 days, and the final yield was 8·5%. Experiments are described which suggest, as did those of Bentley *et al.* (1949), that the toxic substance is a derivative of methionine.

John Yudkin

81. **A Case of Massive Digitalis Poisoning with Recovery.** (Intoxication digitalique massive terminée par la guérison)

G. Bickel, H. Plattner, and H. Edelstein. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **44**, 61–64, Jan., 1951. 6 figs., 7 refs.

A woman of 36 attempted suicide by taking 50 mg. of "digitaline" in a single dose. On the fourth day collapse lasting for 18 hours and associated with a fall in blood pressure from 120/90 to 60/30 mm. Hg occurred, but she recovered. Electrocardiograms showed various degrees of disturbances of A-V conduction, flutter, nodal rhythm, and changes in P waves, but no ectopic rhythms. This observation is published because the dose taken is the largest on record. *A. Schott*

82. **Iron Encephalopathy**

C. A. Birch and M. Till. *British Medical Journal* [*Brit. med. J.*] **1**, 62–63, Jan. 13, 1951. 12 refs.

A case is reported of severe cerebral symptoms in a woman, aged 54, after the intravenous administration of 380 mg. of iron in 9 days. The patient, a housewife, gave a history of increasing dyspnoea and lassitude for 3 years and of oedema of the ankles and soreness of the tongue for 2 months. There had been no previous illness. Her blood pressure was 160/70 mm. Hg, the heart was not enlarged, and although there was a soft systolic bruit over the praecordium, it was not thought to indicate valvular disease. No other abnormality was found. Blood investigation showed a typical picture of severe iron deficiency anaemia.

On the first day of treatment 20 mg., and on the second day 50 mg., of saccharated iron oxide (100 mg. of iron in 10 ml.) was given intravenously. On the third day, after receiving 40 mg., the patient complained of dizziness and that everything appeared "stripy"; she then vomited. However, injections were continued daily, none being greater than 75 mg. On the ninth day of treatment a total of 380 mg. of iron had been administered, and as the patient complained of headache and appeared anxious no injection was given. She later vomited once. In the evening she seemed strange in her manner and drowsy. Later she had a convulsion and became deeply unconscious. Her limbs were flaccid and her eyes were deviated to the right. Her pulse rate was 120 and the rhythm irregular. Further convulsions occurred at intervals of 20 minutes; each affected the left side of her body before becoming generalized. The cerebrospinal-fluid pressure was 230 mm. of water, but laboratory examinations revealed no abnormality. Despite large doses of paraldehyde the convulsions became more frequent until at 1 p.m. next day they were

occurring every 5 minutes. Thereafter they became less frequent and confined to the left side, ceasing at 4 p.m. The patient was unconscious for the next 12 hours. Minute petechiae were present and bruising occurred at the site of pinching. A mild left-sided hemiplegia gradually improved in the next 3 days. The bleeding time was 40 seconds, clotting time 5 minutes, and the platelets numbered 135,000 per c.mm. Four days later the patient was rational and was able to read and write a few words correctly, but unable to understand what she read. The same day she lapsed into a dreamy state which continued for 36 hours. She was discharged after a month, and 2 months later there was no abnormal physical finding, although she was very anxious and easily panicked. The same psychological condition persisted after a further 2 months. An electroencephalogram showed evidence of bilateral damage in the temporo-parietal region.

The saccharated iron oxide was prepared in the usual manner and contained the correct amount of elemental iron and sucrose. It was compatible with the patient's serum, and the LD50 of the sample in mice was approximately 118 mg. per kg., whereas the most suitable preparations were found to have a LD50 of 300 mg. per kg.

The available evidence does not satisfactorily explain the production of cerebral symptoms. It is conceivable that capillary damage sufficient to lead to subsequent damage to the brain might be caused by iron preparations. Animal experiments are quoted. The symptoms are tentatively ascribed by the authors to iron encephalopathy.

[The 36 hours which apparently elapsed between the last dose of iron and the occurrence of convulsions, and the development of paresis confined to the one side (in an anaemic patient who had been in hospital), provide evidence against ascribing this case to "iron encephalopathy". The case is described in detail and further case reports will be awaited with interest.]

R. Hodgkinson

83. **Drug Protection against the Lethal Action of Parathion.** [In English]

P. R. SALERNO and J. M. COON. *Archives Internationales de Pharmacodynamie et de Thérapie* [*Arch. int. Pharmacodyn.*] **84**, 227–236, Dec., 1950. 10 refs.

Several cases of poisoning by the insecticide parathion (*p*-nitrophenyldiethyl thiophosphate), which is a potent inhibitor of cholinesterase, have been reported. In view of the effects of eserine, neostigmine, atropine, and magnesium and calcium salts in poisoning with di-*iso*-propylfluorophosphonate it was decided to investigate their possible prophylactic effects on parathion toxicity. Given by intraperitoneal injection in propylene glycol, this substance (93% pure) has an LD50 of about 5 mg. per kg. body weight in mice, rats, and cats. Previous injection of atropine or eserine increased the LD50 of parathion 8 times in mice and 4 times in cats. Atropine and neostigmine together gave better protection than atropine alone, but neostigmine alone was ineffective in tolerated doses. In mice, magnesium and calcium salts did not give similar protection, but did delay death. They were, however, tested in animals given twice the LD50 of parathion and might have been more effective against smaller doses. Like neostigmine, magnesium sulphate increased the protective action of atropine. If eserine was given after parathion the two drugs acted synergistically as lethal agents.

The degree of protection afforded by eserine appears to be determined by the amount of cholinesterase reversibly bound by the drug before exposure to parathion and serving as a reservoir of enzyme whereby cholinesterase–acetylcholine action can be maintained in the presence of parathion. Survival is possible provided this amount represents 10% or more of the total. The cause of death in atropinized animals eventually succumbing to parathion poisoning is respiratory paralysis, probably due to the unopposed nicotinic action of acetylcholine on skeletal muscle. The fact that neostigmine itself has a strong nicotinic action may be the reason for its being less effective than eserine in prophylaxis against parathion poisoning.

Derek R. Wood

84. **Cachexia due to Immoderate Use of Irritant Laxatives.** (Sur un cas de cachexie dû à l'usage immodéré de laxatifs irritants)

R. CATTAN, R. CARASSO, and P. COTONI. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **66**, 1508–1514, Nov. 17, 1950. 3 refs.

The authors describe the case of an unmarried woman, aged 24 years, who was said to be suffering from pituitary cachexia and was about to undergo ventriculography at the hands of a neurosurgeon. She gave a history of loss of weight (15 kg. in 20 months), amenorrhoea, loss of hair, obstinate constipation, abdominal pain, and vomiting. Her appetite was normal. She had been subjected to intensive hormone therapy. Further inquiry into the history revealed that she had been taking 7 or 8 purgative pills daily, one of which was generally sufficient to provoke violent diarrhoea. This had resulted in 5 or 6 watery stools daily for many weeks. On admission to hospital she was extremely emaciated and dehydrated. Pubic and axillary hair was scanty. The blood pressure was 90/40 mm. Hg. Chvostek's sign was positive, and there was concentric diminution of the visual fields. The blood urea level was 110 mg. per 100 ml., but the urine was normal. Skull and chest radiographs were normal.

All laxatives were stopped. A high-protein diet and subcutaneous saline were given, together with neostigmine 1 ml. and aneurin 100 mg. This resulted in a rapid improvement in a few days, the blood urea level returning to normal and the weight increasing by 7 kg. The temporary appearance of oedema in the lower limbs was attributed to the previous administration of deoxycortone. The amenorrhoea persisted after recovery, as did also the hypotension and Chvostek's sign. The authors regard this condition as due to a functional disturbance of the pituitary which may be reversible.

I. Ansell

Medical Jurisprudence

85. **The Duration of Lesions Produced by Instruments Commonly Used for Grasping and Immobilizing the Cervix *per vaginam*. A Medico-legal Contribution to the Diagnosis of Criminal Abortion.** (Sulla durata delle lesioni prodotte dai più comuni strumenti atti ad afferrare il collo dell'utero per via vaginale e ad immobilizzarlo. Contributo medico-legale alla diagnosi dell'aborto criminoso)
F. SPIRITO. *Athena* [*Athena, Roma*] **16**, 239–241, Nov., 1950.

The author complains that criminal abortion is becoming more common in Italy every day. Often the woman herself is responsible for it, by introducing simple instruments, such as a knitting-needle, through the os. If the abortion has been performed by a doctor, he will probably have used an instrument to pull down the cervix. The finding of a cervical lesion caused by such an instrument may therefore be of medico-legal importance. The author studied many such cases and found that typical lesions may be seen during the subsequent 3 days. *R. d'Amico*

86. **Medico-legal Aspects of the Treatment of the Sexual Offender, with Discussion of a Method of Treatment by Gland Extracts**
R. S. HODGE. *Medico-Legal Journal* [*Med.-leg. J.*] **18**, 130–144, 1950. 14 refs.

It is agreed by most psychotherapists that for the treatment of a sexual offender some degree of "fluid anxiety" must be present or the prognosis is not good. The author's experience has been that this "fluid anxiety" is often lacking, and there is a real reluctance to accept a psychotherapeutic approach to the difficulty and a tendency to cling to the aberration in spite of the social problem which it raises and the persistent risk of re-conviction.

Amongst young persons, heterosexual offences may be due to no more than an ignorance of simple, fundamental physiology, accompanied by intellectual dullness, lack of parental control, and improper introduction. The rapid onset of puberty may not be accompanied by appropriate mental development, and a state of temporary imbalance of instinctual drive may overwhelm higher inhibition. Study of a group of homosexual adult males leads the author to the conclusion that the great majority are true deviants from the heterosexual pattern in whom this deviation has been present from an early age; that it is as much their form of sexuality as heterosexuality in the majority; and that heterosexuality is as repugnant to them as homosexuality is to the heterosexual. A distinction must be drawn between those who are licentious and vicious and those who are deeply concerned about their abnormality. The former type is a menace and must be restrained, but temporary committal to the homosexual environment of prison is probably not the correct solution. The second type presents a difficult medical problem; the author feels that the true homosexual is not amenable to psychotherapy. Similarly in the case of many crimes of violence committed with a sexual motive psychotherapy seems to be relatively useless. In Denmark, castration is held to supply the solution, but potency may remain after castration in adult life; in some persons a reflex pattern of sexual behaviour survives in the central nervous system and suffices to enervate the penile mechanisms. Thus a sexual criminal after castration may continue to be a social nuisance. Patients with acromegaly treated with large doses of oestrone were found to lose sexual power after 14 days, but a maintenance dose was necessary to prevent the return of libido; 15 sexual offenders have been treated by this method and sexual appetite completely abolished. The difficulty of controlling the patient who discontinues treatment after a period is recognized. *Gilbert Forbes*

87. **Examination of the Complaining Witness in a Criminal Court**
L. L. ORENSTEIN. *American Journal of Psychiatry* [*Amer. J. Psychiat.*] **107**, 684–688, March, 1951. 6 refs.

The author was formerly psychiatrist-in-charge of the Psychiatric Clinic, Court of General Sessions, New York City, and his department had to examine annually some 3,000 persons convicted of felony. He considers that in many instances not only should the accused undergo a psychiatric examination, but the complainant witness also. He has rarely had an opportunity of examining the complainants, but such an opportunity did present itself in a few cases of sexual crime. He reports 3 of these cases, in which complaints made against men were shown to be fabrications when the girls were closely questioned.

[Skilful interrogation by an experienced police officer, in the absence of medical corroboration, ought to have produced the same result in 2 of the cases at least, and should have resulted in no charge being preferred at all.] *Gilbert Forbes*

88. **Malignant Disease in Relation to Sudden Death.** (Das Verhalten der malignen Geschwulste zum plötzlichen Tod)
J. GERINGER. *Klinische Medizin* [*Klin. Med., Wien*] **5**, 566–576, Dec. 1, 1950.

Sudden death was observed in association with malignant disease in 72 cases, or in about 2·5% of cases examined. The cause of death was asphyxia due to occlusion of the respiratory passages, fatal haemorrhage from erosion of major blood vessels, peritonitis following perforation of the bowel or female genital organs, oedema of the brain and increased intracranial pressure, or increasing cachexia due to widespread metastases. *R. Salm*

See also Section Pharmacology and Therapeutics, Abstract 79.

Radiology

89. **Experimental Confirmation of a Previously Reported Unusual Finding in the Blood of Cyclotron Workers**
M. INGRAM and S. W. BARNES. *Science* [*Science*] **113**, 32–34, Jan. 12, 1951. 1 fig., 1 ref.

The authors have previously reported the appearance of lymphocytes with double bilobed nuclei in the blood of subjects associated with the cyclotron at the University of Rochester after exposure below accepted tolerance levels. The experiments in 3 dogs which are recorded in the present paper confirm these findings.

Daily blood studies were carried out for 2 months before the experiment and only one blood smear was found to have one or more lymphocytes with bilobed nuclei. No other blood abnormalities were found. The dogs were then fastened 50 feet (15·2 m.) from the target, and well outside the neutron beam, for 30 minutes while the cyclotron was operating. Each dog was exposed once in each of three positions. Although the radiation received was not measured it was believed that the exposures were well below the currently accepted tolerance levels. Approximately 180 blood smears were examined during the first week after exposure and then 30 smears each week. The experiment was continued for one year. Lymphocytes with bilobed nuclei were found in about 20% of the smears during the first and second weeks, and in a diminishing number during the succeeding weeks. After the sixth week the characteristic cells were not found.

Although bilobed lymphocytes are not diagnostic of radiation effects, it is important to note that these changes in the blood were produced by very small exposures. Such changes may suggest that slight exposure is occurring and may indicate that a particular operation is potentially dangerous before more obvious changes appear in the blood of the subjects involved.

T. M. Pollock

90. **The Effect of Variation in Dosage Rate of Roentgen Rays on Survival in Young Birds**
S. P. STEARNER. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 265–271, Feb., 1951. 4 figs., 6 refs.

Unsexed Leghorn chicks and mammoth white Pekin ducks were subjected to total body irradiation. The chicks were divided into groups on the basis of age at the time of irradiation; all ducks were 2 to 3 days old. The rate at which the dose of radiation was given varied from 6 r per minute to 43 r per minute. It was found that survival following total body irradiation depended on the total dose, dose rate, and age at the time of exposure.

In newly-hatched chicks given a dose of 1,000 r at 15r or more per minute the mortality was 75% within 24 hours, but if exposed to the same dose at 6 r per minute the mortality within 24 hours was only 1%, although 46% died between 5 and 10 days after irradiation. One-week-old chicks were exposed to the same dosage of x rays: there was little difference in the shape of the survival curve for doses given at 6 r and at 43 r per minute, but the largest number of deaths occurred in the first 24 hours. Irradiation of 2-week-old chicks resulted in a large percentage of early deaths after exposure at 43 r per minute, but a relatively uniform death rate after exposure at 6 r per minute. The 2- to 3-day-old ducks reacted in a similar way to the 2- to 3-day-old chicks, suggesting that the dose-rate effect on survival may be characteristic of the avian class.

It is suggested that recovery is taking place during exposure at the low rates, so that the total effect of the dose is less than if it were given at a high rate. The mechanism leading to early death, however, is not clearly understood.

J. J. Mathews

91. **Effect of Roentgen Rays on the Testis. Quantitative Histological Analysis following Whole Body Exposure of Mice**
A. B. ESCHENBRENNER and E. MILLER. *Archives of Pathology* [*Arch. Path.*] **50**, 736–749, Dec., 1950. 7 figs., 13 refs.

A review is given of previous work and theories dealing with the effects of irradiation on the components of mammalian testes. The present paper is a sequel to some previous work by the same authors on the irradiation of mice by γ rays, which suggested that chronic irradiation results in retardation of the rate of multiplication of spermatogonia, with minimal cell death. In the present experiments mice were given whole body irradiation of 50 to 400 r at 186 kV and serial studies were made of the testes: in some cases a second dose was given after recovery from the first. Results from the 10-MeV betatron are also included.

Full details are given of experimental procedures and results. Very clear photomicrographs illustrate the results obtained. Serial studies from one to 6 weeks after irradiation showed the main effect, as previously observed, to be on the rate of maturation of spermatogonia. The same effect was seen when a second dose was given after recovery from the first and also when the betatron was used. Injury and recovery seemed to run parallel with loss of, or increase in, weight of the organ and were in proportion to the dose given. This relationship to the dose also held for the time taken to reach the minimum weight and the time for the testis to return to normal.

This experiment confirmed the observations made in the previous one. There was again almost complete absence of cell death even at the higher doses, and the effect did not appear to be " all-or-none ". Since the second irradiation followed the pattern of the first there

would appear to be no residual metabolic damage following sublethal irradiation.

As division of spermatogonia is considered to be similar to that of somatic cells a further experiment has been started to find out whether a similar radiation effect is obtained. *V. M. Dalley*

RADIOTHERAPY

92. **Irradiation Damage of the Intestines following 1,000-Kv Roentgen Therapy. Evaluation of Tolerance Dose**

H. I. Amory and I. B. Brick. *Radiology* [*Radiology*] **56**, 49–57, Jan., 1951. 5 figs., 13 refs.

Abdominal radiation was delivered to 20 patients with seminoma testis. Two pairs of opposing fields, 10 × 10 cm. or 10 × 15 cm., were used and doses, calculated in the region of the transverse colon, of 4,500 to 11,000 r were given: the duration of treatment varied from 27 to 126 days. As much as 7,000 r was given in 27 days. Of the 20 patients, 12 are dead, all having damage to the intestine. Of the living, 3 have radiological evidence of damage and 5 are without symptoms and have not been examined. The damage may include peritoneal adhesions, shortening of the colon and small intestine and shortening of their mesenteries, thickening and rigidity of the wall of the gut, and ulceration and perforation. There was some correlation between dose and extent of the damage: it is concluded that a dose of 4,500 r in 54 days would be tolerated by the intestine.

J. Boland

93. **Late Radiation Reaction in the Small Intestine Manifest Eight Years after Therapy. Report of a Case**

R. C. Frank and E. A. Pohle. *Annals of Surgery* [*Ann. Surg.*] **133**, 104–108, Jan., 1951. 4 figs., 7 refs.

An adenocarcinoma of the colon in a woman of 24 is reported; a late radiation reaction developed in the small bowel, requiring surgical resection 8 years later. The tumour was first removed in March, 1938, recurred, and again removed in February, 1940. As it was a highly anaplastic tumour, recurring in a young woman, post-operative irradiation was administered. A second course was given when a further mass was felt in June, 1940, and a third in January, 1941. In January, 1949, resection of a constricted segment of terminal ileum was carried out for late radiation stricture with telangiectasia, fibrosis, and oedema. *D. Waldron Smithers*

94. **The Principles of Treatment by Radiotherapy in Breast Carcinoma**

R. McWhirter. *British Journal of Cancer* [*Brit. J. Cancer*] **4**, 368–371, Dec., 1950. 3 figs., 1 ref.

Results of surgical treatment of breast cancer are good so long as the disease is confined to the breast. Spread to the axilla is commonest, but the supraclavicular nodes are involved in 33% of cases where axillary nodes are involved, while in a high proportion lymph nodes are involved along the internal mammary artery.

There are five main principles in the treatment of breast cancer by radiotherapy.

(1) The axillary and supraclavicular lymph nodes must be treated as one continuous chain. From experience with tuberculous lymph nodes it can be demonstrated that the carotid and posterior cervical chains are continuous with the nodes of the axilla, and that the medial supraclavicular nodes are in fact the proximal group of the axillary chain. In carcinoma of the thyroid, when the neck nodes are involved it is common to find that there is also axillary involvement. This continuity is also demonstrable in patients with metastatic nodes from a primary growth in the naso-pharynx. It follows, therefore, that the axillary and supraclavicular nodes must be treated as one continuous chain by two directly opposed fields, one anterior and one posterior. Separate axillary and supraclavicular fields leave a gap which must be irradiated to ensure success.

(2) The internal mammary lymph nodes must be treated in continuity with the chest wall. This is done by the use of glancing chest fields, the medial extending beyond the midline and angled to avoid lung damage. If the separation of these fields is over 16 cm. an adequate dose cannot be delivered. The use of large fields and bolus ensures even distribution, and gaps between adjacent fields must be avoided.

(3) Hard-quality radiation is essential. In Edinburgh, recurrences in the axilla are much commoner when a beam of H.V.L. 1·6 mm. copper is used than when the standard beam of H.V.L. 3·7 mm. copper is used.

(4) Adequate dosage throughout the whole treated area. The minimum is 3,750 r in 3 weeks, and the maximum permissible is 4,500 r. If 3,750 r cannot be delivered, it is better to carry out radical operation.

(5) Only one course of treatment is permissible.

In 1,345 cases treated at the Royal Infirmary, Edinburgh, in the years 1941 to 1945 the 5-year survival rate was 43·7%. Among the 757 operable cases the 5-year survival rate was 62%, whereas among the 389 inoperable cases, locally advanced, the 5-year survival rate was 29%. For the 1,146 patients without evidence of distant metastases the 5-year survival rate was 50·5%.

I. G. Williams

95. **Cancer of the Breast. Results of Treatment, 1929 to 1943.** [In English]

J. Saugmann-Jensen and P. Jacoby. *Acta Radiologica* [*Acta radiol., Stockh.*] **34**, 453–468, Dec., 1950. 23 refs.

Opinions vary concerning the correct treatment of carcinoma of the breast, and the results obtained at Odense Radium Centre from 1929 to 1943 are published in order to contribute to the discussion on the indications for *x*-ray therapy and surgical treatment. Both these forms of treatment can be expected to affect only the primary manifestations, whereas the outcome of the disease depends on distant metastases, of whose form and intensity a definite view can never be formed in advance. Radical mastectomy was performed on 289 patients; 40% were alive after 5 years; 159 had pre- and post-operative *x*-ray therapy, 130 post-operative *x*-ray therapy alone. There was no great difference in survival

rates (37% and 42% respectively). Local recurrences in the flaps occurred in 11% of the pre- and post-operative *x*-ray therapy group, and in 17% of the post-operative *x*-ray therapy group.

A total of 489 patients were treated altogether, 330 by surgery and 159 by *x*-ray therapy: 30% of the 489 were alive after 5 years, 20% being symptom-free. On comparison with similar cases recorded in the world's literature, no demonstrable effect of supplementary *x*-ray therapy is found in this series. Only 18% had no recurrence after 10 years, a fact which shows how little the 5-year results can tell about permanent recovery in carcinoma of the breast. From 1929 to 1938 the 5-year survival rate was 27%, whereas from 1939 to 1943 it was 41%. No explanation can be found for this improvement, as similar techniques were employed. Out of 41 patients subjected to simple mastectomy and irradiation 27 were alive after 5 years, a figure which raises the question whether better results might not be obtained in a number of cases by local operation and irradiation rather than by radical mastectomy.

Examination of the voluminous literature on carcinoma of the breast in connexion with this analysis suggests that treatment has become stagnant at a not very satisfactory level. Supplementary *x*-ray therapy does not seem to have caused any signal improvement, and it is not known what combination of surgery and radiotherapy is to be preferred, although supplementary irradiation may reduce local recurrences. Only 1 patient in 3 is alive, and 1 in 5 symptom-free, after 5 years. Radical operation is superfluous if there are no axillary metastases, whereas it may be harmful if there are cancerous axillary lymph nodes. The first step towards better results is undoubtedly a world-wide, uniform, statistical analysis.

I. G. Williams

96. **Post-irradiation Haemorrhage of the Pituitary.** (Radiohemorrhagie hypophysaire)
T. LEHOCZKY. *Archivio Internazionale di Studi Neurologici* [*Arch. int. Studi neurol.*] **1**, 31–34, Dec., 1950. 15 figs., 24 refs.

A chromophobe adenoma of the pituitary in a woman of 47 was subjected to *x*-ray treatment (total 5,000 r) with improvement in 1947. In 1949 she relapsed, with visual failure and headache. She was also found to have achylia gastrica and a hyperchromic anaemia. She was treated with liver extract and further *x* rays to the pituitary (total 1,350 r). After the ninth treatment she became ataxic, with vertigo and nausea, and 3 days later she died in coma. Necropsy showed oedema with multiple haemorrhages into a chromophobe adenoma 4 × 4·5 cm. in size, and herniation of the hind-brain into the foramen magnum. From the histological changes present, the author presumes the haemorrhages into the tumour to have resulted from the following factors: changes had been caused in the walls of the vessels of the tumour by the previous *x*-ray treatment in 1947, which rendered them more sensitive to an accelerated reaction to the further course of radiotherapy; and secondly, the pernicious anaemia [*sic*] caused a super-added haemorrhagic tendency. There is a brief review of the literature, and the author concludes that the presence of any condition predisposing to haemorrhage constitutes a contraindication to *x*-ray therapy of the nervous system.

[The author does not mention any clinical evidence of bleeding tendency in this patient during life, and none was found in other organs at necropsy.]

J. B. Stanton

97. **Supraspinatus Tendinitis. A Survey of 300 Consecutive Cases Treated by Roentgen Therapy**
O. T. STEEN and J. A. L. MCCULLOUGH. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 245–254, Feb., 1951. 2 figs., 26 refs.

Supraspinatus tendinitis, a synonym for subacromial or subdeltoid bursitis, is described as a primary degenerative process associated with a chronic inflammatory reaction involving one or more components of the tendon-capsule cuff. The authors discuss the pathogenesis and diagnosis of this incapacitating lesion and refer to the very extensive literature. An analysis is made of 300 consecutive cases treated by *x*-ray therapy. Males and females were equally affected, the average age being 50 years. The effects of *x*-ray therapy are considered to be mainly due to the induced hyperaemia, increased blood and lymph flow resulting in resorption of toxic materials, and the mobilization of antibodies. The normal course of treatment was 150 r (air) daily for 4 days, with a 10 × 10 cm. port at 50 cm. focus–skin distance and 200-kV *x* rays filtered by 0·5 mm. Cu and 1 mm. Al. In acute cases some initial exacerbation of symptoms was not uncommon. An effort was made to classify the response to treatment, and the authors claim either complete or almost complete remission of symptoms and signs in 83·6% of cases. The duration of these remissions is not stated, and a 39% recurrence rate is admitted after one course of treatment. No significant difference in response was noted in cases having a definite history of injury, nor was there any significant difference in those having radiological evidence of calcium deposits. One sub-group of patients, in whom previous therapy of various types had been employed, responded less favourably to *x*-ray therapy than the remainder of the series.

E. C. Easson

98. **Thorium X Treatment of Skin Epithelioma, Keratoses, and Delayed Radiation Changes**
J. J. SHER and W. E. HOWES. *Radiology* [*Radiology*] **56**, 39–48, Jan., 1951. 16 refs.

The α rays from thorium X represent 99% of the total energy emitted. Measurements have shown that these should be able to penetrate only 0·08 mm. into the skin, but it seems that their effects are perceptible to a depth of 0·3 mm. This may be due to absorption of the alcoholic base and to diffusion of the gaseous first decay product into the skin. However, in spite of this small penetrating power, 46 basal-cell carcinomata, 4 squamous-cell carcinomata, and one baso-squamous carcinoma have been successfully treated with thorium X, there being failure only in a basal-cell carcinoma involving bone.

A concentration of 300 μc (2,000 e.s.u.) per ml. of alcohol or per gramme of lanoline was used; this was

applied in 8 weekly treatments. An erythema appeared a few days after the first treatment and the tumour gradually resolved without moist desquamation. The cosmetic results are described as very good. No severe scarring or telangiectasis has been seen.

Thorium X is recommended also for treatment of radionecrosis and telangiectasis. *F. Batley*

99. **Simultaneous Symmetrical Paired Comparison Method of Evaluating Results of Grenz Ray and of *X*-ray Therapy**

S. L. Hanfling and I. H. Distelheim. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **16**, 65–70, Jan., 1951. 1 fig., 16 refs.

The advantages of grenz rays in the treatment of superficial dermatoses are discussed. To compare the therapeutic effect of grenz rays and *x* rays 24 patients with bilateral symmetrical eruptions were treated, the results with grenz rays on one side being compared with those with *x* rays on the other. The dose of grenz rays was 190 to 220 r (H.V.L. 0·024 mm. and 0·028 mm. Al at 12 and 14 kV respectively) given on 3 to 21 occasions once or twice weekly. On the other side 100 r of *x* rays at 95 kV (H.V.L. 0·9 mm. Al) was given at weekly intervals for 2 to 15 doses (usually 3 to 5).

It was found that in 21 out of 28 courses of treatment (4 patients relapsed and had further treatment) the two types of ray produced similar results, and that in 6 of the remaining 7 there was a better response to grenz rays than to *x* rays. *S. T. Anning*

RADIODIAGNOSIS

100. **The Technique of Radiological Enlargement.** (La technique d'agrandissement radiologique)

G. J. Van Der Plaats. *Journal Belge de Radiologie* [*J. belge Radiol.*] **33**, 89–114, 1950. 15 figs.

The author recalls the relation to the size of the focal point of an *x*-ray tube of the sharpness of the radiograph and also to the distance from the object to the screen. The nearer the object is to the tube, and the farther from the film, the larger the shadow which it casts. If a fine rotating anode is used, an enlarged radiograph, which is also sharp, can be produced.

The blurring (lack of sharpness) of an *x*-ray image is composed of: (1) the geometric blurring (caused by the focal spot), (2) the movement blurring (caused by the movement of the object during the exposure), and (3) the screen lack of sharpness (caused by the dimensions of the grain of the screen). With a very small focal spot (1) can be neglected and the distance between focal spot and object decreased, whereas the object–screen (film) distance can be increased. The result is an enlarged *x*-ray image. Details that are not seen in an ordinary *x*-ray film (infraliminar) become visible by this (supraliminar) technique. There is an increase of contrast, because a great part of the scattered radiation does not reach the screen (or film).

Fluoroscopy with enlargement makes quicker observation possible. Special precautions have to be taken to avoid giving too high a skin dose. By using higher tensions (up to 125 kV) a considerable decrease in exposure time and/or in the size of the focal spot is possible. With a 0·3-mm. rotating-anode tube and a 125-kV apparatus it is possible to obtain enlarged pictures from several parts of the body with very rapid exposures. For equal contrast at various tensions it is essential that the " exposure dose " on the film be constant.

The enlargement technique in *x*-ray work may be used for various regions. The distance between the tube and the cassette is 90 cm. The tube can be placed up to 20 cm. from the patient. The cassette is then displaced so that the total distance from tube to cassette remains 90 cm. The amperage and voltage to be put through the tube are calculated according to the formula $E = kV^5 \times mAS$, E being the intensity on the film. Thus if a radiograph is normally taken with 60 kV and 100 mAS, it will be obtained in the enlargement technique with 120 kV and 3 mAS. A very small focus is indispensable. Some years hence it may be possible to obtain foci even smaller than the present ones. *G. Vilvandré*

101. **Shortening of the Posterior Wall of the Sella Turcica Caused by Dilatation of the Third Ventricle or Certain Suprasellar Tumors**

B. S. Epstein. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 49–55, Jan., 1951. 4 figs., 5 refs.

In order to determine the significance and the cause of the finding of shortening of the posterior wall of the sella turcica, the *x*-ray appearances in 150 normal subjects and 246 patients with intracranial pathology were reviewed. The abnormal cases included 34 of hydrocephalus and 82 of tumours in the region of the sella. The author's conclusions support Twining's observation that shortening of the posterior wall of the sella may be due either to erosion by a parasellar tumour or to pressure from a hydrocephalic third ventricle. The sella was enlarged in every case due to hydrocephalus; the author therefore considers that shortening of the dorsum without sellar enlargement is always due to a local tumour. Air studies of the third ventricle in the hydrocephalic cases showed this structure to be draped across the shortened posterior clinoid processes and extending downward behind them, sometimes as far as the pontine cistern. Such a downward extension constitutes a hitherto unrecorded type of transtentorial herniation of the third ventricle.

[The conclusion that a hydrocephalic third ventricle never produces shortening of the posterior clinoid processes without expanding the sella is open to doubt. In his article on the third ventricle Twining (*Brit. J. Radiol.*, 1939, **12**, 385 and 569) states that it can occur and shows line drawings of a case in which it was seen.] *J. A. Shiers*

102. **Intracranial Calcification in Toxoplasmosis**

D. Sutton. *British Journal of Radiology* [*Brit. J. Radiol.*] **24**, 31–37, Jan., 1951. 8 figs., 14 refs.

Although the positive diagnosis of toxoplasmosis can be made only by demonstrating the organism in body

fluids or in human tissue obtained at biopsy or necropsy, the detection of specific antibodies in the blood serum has proved of great diagnostic value, particularly when associated with the presence of such antibodies in the patient's mother. In the majority of reported cases there is evidence of intracerebral calcification. In the minority, where there is no evidence of such calcification, radiology is of no diagnostic significance. The 6 cases here reported all showed multiple areas of calcification in the skull, often subcortical and frequently involving the basal ganglia. The calcification may take various forms, but the presence of linear or curvilinear streaks is thought to be very suggestive of toxoplasmosis.

In considering the differential diagnosis, mention is made of 3 cases of torulosis which showed calcification of similar distribution, but without curvilinear streaks. The finely granular, symmetrical calcification occurring in the basal ganglia in hypoparathyroidism must be remembered. With cysticercosis there should be no real confusion, as in this condition the calcifications are tiny, uniform in size and density, and evenly distributed. Calcification in arteriosclerotic cerebral vessels also gives a characteristic appearance. Tuberous scelerosis may also give rise to multiple opacities, but they are, as a rule, much fainter than those caused by toxoplasmosis and again do not show the curvilinear streaks. In cases showing only single calcifications radiological diagnosis is less certain, though the radiological findings may have a limited value as confirmatory evidence.

L. G. Blair

103. **Familial Fibrous Swelling of the Jaws**
J. CAFFEY and J. L. WILLIAMS. *Radiology* [*Radiology*] **56**, 1–14, Jan., 1951. 6 figs., 15 refs.

The clinical and *x*-ray findings in 5 members of two families with this rare condition are described. The 2 children had progressive painless swellings of the cheeks and jaws: the others were the 14-year-old sister and the mother of one child, and the father of the other. All had a history of a similar condition in childhood which had improved as they grew older.

The patients were apparently normal at birth; one was proved radiologically to be so. The condition appeared during the first 3 years, progressed rapidly for 2 to 3 years, and then progressed more slowly or became static. At the age of 10 it started to improve, so that the adults showed no obvious external abnormality. At the height of the disease there was gross facial deformity due to swelling of the bone of the maxilla and mandible. This interfered mechanically with swallowing and with closure of the mouth; in one case it caused backward displacement of the tongue which threatened to produce respiratory obstruction. Dentition was defective in all subjects. Radiologically, the bone of the maxilla and mandible was rarefied and expanded. In the maxilla the changes were diffuse and even, in the mandible well-defined; multilocular cystic areas were present. No other bones were affected. After puberty these changes regressed progressively, so that by middle age they were no longer apparent.

The histological and *x*-ray findings in the jaws are identical with those of fibrous dysplasia, but the familial history and the extensive involvement of the jaws without changes in other bones permit the condition to be distinguished clearly.

J. A. Shiers

104. **Measurement of Heart Size**
G. BOURNE and B. G. WELLS. *Lancet* [*Lancet*] **1**, 17–18, Jan. 6, 1951. 1 fig., 1 ref.

A simple method of rapid measurement of the diameter of the heart is described: it is based upon orthodiagraphic technique. The *x*-ray apparatus must be of the type which permits lateral movement of the tube independently of the screen. The shutters are set to leave only a vertical slit of about 1 inch (2·5 cm.) in width and this is moved until it registers with each border of the heart in turn, a line being drawn on the screen at a tangent to the cardiac border. Accuracy was checked by making three separate measurements on each of 53 patients, the measurements not being consecutive and the operator being unaware of the identity of the subject. Only in 4 of these patients did the difference between the highest and the lowest reading of the cardiac width prove to be more than 0·6 cm. An investigation into the possible error introduced by slight obliquity of the patient revealed that this position would produce a significant change in measurement in only a small proportion of cases, and then only when obliquity was such as to be fairly readily detectable by the hands of the examiner.

This method is advocated as a simple and valuable adjunct to the clinical examination of the heart.

A. M. Rackow

105. **Radiokymographic Findings in Congenital Heart Disease.** (Röntgenkymographische Befunde bei kongenitalen Herzfehlern)
P. THURN. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **74**, 151–159, Feb., 1951. 6 figs., 12 refs.

In congenital valvular diseases of the heart radiokymography may help in the accurate interpretation of the observed changes in the outline of the various segments of the heart. Deneke's sign does not necessarily indicate a defect in the ventricular septum; it is rather a sign of the "single ventricle". A projecting conus pulmonalis has been identified, by means of cardioangiography, as the pulmonary artery. It may show intermediary diastolic prongs in cases of patent ductus arteriosus. Stenosis of the isthmus is characterized by increased amplitude in the prestenotic segment and decreased amplitude in the post-stenotic segment. The differential diagnosis by means of kymography between hilar infiltration and ectatic hilar vessels is discussed.

A. Orley

106. **Retrograde Aortography with a Special Catheter, including Demonstration of the Coronary Arteries**
F. PEARL, N. GRAY, and B. FRIEDMAN. *Annals of Surgery* [*Ann. Surg.*] **132**, 959–964, Nov., 1950. 5 figs., 9 refs.

A technique is described for demonstrating selected portions of the aorta and its main branches by retrograde arterial catheterization. A special, narrow, opaque

catheter with a curved tip is used (inside diameter 0·59 mm., outside diameter 2·5 mm.). The proximal portion of either the radial or profunda femoris artery is exposed, and the catheter is introduced and passed into the appropriate part of the aorta under screen control: 4 to 10 ml. of 70% diodone is injected through the catheter as quickly as possible by hand and two films are taken as rapidly as possible 1½ seconds after the start of the injection. The catheter may be kept in position until satisfactory films have been obtained provided that saline solution is injected through it slowly between injections of contrast medium. In order to prevent clotting, a steady trickle of saline must be maintained the whole time it is in the arterial lumen. At the conclusion of the examination the catheter is withdrawn and the arterial wall repaired with sutures.

In this way satisfactory arteriograms of the thoracic aorta and its main branches, including the coronaries, may be obtained through the radial artery, and of the abdominal aorta and its cardiac, mesenteric, and renal branches through the profunda femoris. It is claimed that the small amount of contrast medium needed reduces the risk of reactions to diodone, and that more satisfactory films are obtained because the dye-filled arteries are seen against a background unclouded by excess opaque medium in other vessels.

The method has been used mainly on dogs. So far it has only been used on one human subject, when satisfactory arteriograms of the ascending aorta, aortic arch, and the left subclavian artery were obtained without ill effects. *J. A. Shiers*

107. **Isthmic Stenosis of the Aorta.** (Die Isthmusstenose der Aorta)
A. VOGT. *Fortschritte auf dem Gebiete der Röntgenstrahlen* [*Fortschr. Röntgenstr.*] **74**, 159–173, Feb., 1951. 21 figs., 8 refs.

A report is given of 10 cases of stenosis of the aortic isthmus, all of which were diagnosed clinically in the first instance. In some of the patients an aneurysm above the stenosis could be demonstrated by means of kymography, although it was not possible to locate the stenosis in every case by kymography in the oblique projection. An aneurysmal dilatation of the innominate artery may frequently be detected by kymography. Even a slight isthmic stenosis may cause severe disability and considerable hypertension in the upper half of the body. Neither the location of erosion of the ribs nor the number of the ribs eroded is of help in the location of the exact site of the stenosis. *A. Orley*

108. **Translumbar Aortic Puncture and Retrograde Catheterization of the Aorta in Aortography and Renal Arteriography**
W. E. GOODWIN, P. L. SCARDING, and W. W. SCOTT. *Annals of Surgery* [*Ann. Surg.*] **132**, 944–958, Nov., 1950. 12 figs., 21 refs.

Experiences in abdominal aortography are described. Translumbar aortic puncture has been employed for 2 years. The technique employed is orthodox except that needles of rather wide bore are used; a spinal or general anaesthetic is always given. Sodium iodide (80%), diodone (70%), "thorotrast", and "neo-iopax" (75%) have been tried as contrast media: there seems little to choose between them.

A descending pyelogram is always carried out the day before the aortography; this serves to exclude iodine sensitivity. The method has been used successfully on children, including one aged 18 months. No complications are recorded; in 2 cases dye was injected into the soft tissue outside the aorta without ill effects.

Retrograde catheterization of the abdominal aorta has been carried out 15 times. An ordinary ureteric catheter is introduced into the lateral circumflex branch of the profunda femoris artery and passed up for 35 cm.; the artery used is ligated distally and has to be sacrificed. An exposure is made during the injection of 4 to 5 ml. of contrast medium to check the position of the catheter, and if this is satisfactory further films are exposed after the injection of 30 ml. and 40 ml. of contrast medium. In order to prevent clotting, it is necessary to inject saline slowly through the catheter the whole time it is in the arterial lumen. The method gives satisfactory results, but is sometimes tedious and time-consuming. No serious complications have occurred, but a number of mishaps are reported. In one case the catheter was pushed through a diseased arterial wall into the perivesical tissues and withdrawn again without apparent ill-effect. In another, the patient complained of weakness of his leg, presumably due to interference with the blood supply.

Both methods have proved safe and useful procedures, though unlikely to become routine techniques. The greatest difficulty at present is in interpretation of the angiograms. Once the technique of tapping the aorta has been learned, translumbar aortic puncture has been found to be quicker, simpler, and safer than retrograde catheterization. Catheterization may prove useful in special cases, for example, in the investigation of aortic aneurysms, to obtain selective filling of segments of the aorta, and possibly in the examination of the thoracic aorta. Its full possibilities have yet to be worked out. *J. A. Shiers*

109. **The Diagnostic Value of Dynamic Studies in Angiocardiography. Evaluation of New Rapid Technique**
T. F. KEYES, C. WEGELIUS, and J. LIND. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **21**, 164–171, Feb., 1951. 5 figs., 7 refs.

110. **A Water-soluble Contrast Medium for Bronchography. Report on Clinical Use**
R. J. ATWELL and R. L. PEDERSEN. *Diseases of the Chest* [*Dis. Chest*] **18**, 535–541, Dec., 1950. 3 figs., 13 refs.

"Viscous umbradil B" is a water-soluble contrast medium consisting essentially of "iodopyracet" (diodone), sodium carboxymethylcellulose, and a local analgesic ("xylocaine"). Diodone is the diethanolamine salt of 3 : 5-diiodo-4-pyridone-N-acetic acid. The most satisfactory mixture was one containing 50% of diodone, 3·3% sodium carboxymethylcellulose, and 0·5%

xylocaine; but the viscosity can be varied according to need by varying the percentage of sodium carboxymethylcellulose.

For bronchography the medium is instilled into the trachea through a nasal catheter in the usual way, but preliminary anaesthetization of the larynx and trachea is more important than when using oily contrast media, as viscous umbradil is rather more likely to produce coughing. The contrast obtained is slightly less than with oils, but this can be compensated for by the *x*-ray technique. Speed in the taking of films is necessary, as there is a tendency for the medium in the upper lobes to flow into the lower. The advantage of this medium is that it is rapidly absorbed and excreted by the kidneys. Five hours after bronchography no trace of it can be seen in the lungs on *x*-ray examination. It therefore does not remain to confuse and render difficult the interpretation of future radiographs as do the iodized oils. Moreover, bronchography can, if desired, be repeated at frequent intervals. Viscous umbradil does not seem to cause any appreciable irritation or damage to the bronchi and lungs, but as it is excreted by the kidneys its use is contraindicated by the presence of nephritis.

[This medium would seem to merit further trial, though the technique of its use seems rather more tricky than that required for " lipiodol ". The illustrative bronchograms reproduced in this paper are only fair.]

John Forbes

111. **Tissue Changes in the Lungs after Bronchography with " Ioduron B ".** (Veranderungen des Lungengewebes nach Bronchographien mit Joduron B)
W. VISCHER. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **81**, 54–58, Jan. 20, 1951. 4 figs., 11 refs.

Pathological changes in the lungs following bronchography with oily suspensions of iodine have long been recognized and " lipiodol " itself was held to be responsible. In 1948 Fischer and Mülly introduced a watery suspension containing 50% iodine and made viscous by the addition of cellulose-ethyl-glycolic acid. In animals this medium was fully absorbed after 24 hours and was radiologically invisible after 3 to 4 hours, but histological changes were present which could not be adequately explained. To investigate this the author injected " ioduron B " into the bronchial tree of animals. As the medium was not visible after a short time it was thought that the cellulose-ethyl-glycolic acid might be responsible. This was therefore injected separately into rats and guinea-pigs. It was found that the changes were identical to those produced by ioduron B. When the animals were killed immediately after the injection, the medium was mostly in the bronchi, and a few erythrocytes were present in the alveoli. Lung-tissue changes did not occur until the end of one hour, when there was a blood-stained exudate with lymphocytes and leucocytes around the medium. After 24 hours the alveolar septa were widened, with multiplication of leucocytes and fibroblasts; large mononuclear cells were also present. The reaction began to decrease at the end of 8 days. The injected material was still present at the end of 4 months.

These findings are at variance with those of other workers who, after a week, were able to demonstrate only a few granules of phagocytosed material; in the present series a distinct phagocytosis could be demonstrated after 24 hours, and after 4 months a considerable quantity of medium was still present. These differences may be partly due to the use of thionin tartrate as a stain in place of toluidine blue. The advantage of ioduron B over lipiodol is that it does not leave behind any radiological signs, but the histological changes are equally marked, both producing a foreign-body tissue reaction. There appears to be an individual susceptibility, as the reaction varies in different cases. In view of these findings the indications for bronchography should be carefully considered. *John H. L. Conway-Hughes*

112. **Bronchography in Children**
E. RIVERO. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 173–179, Feb., 1951. 14 figs., 5 refs.

During a study of the bronchial lesions in children suffering from primary tuberculosis and its sequelae the limitations of bronchoscopy in small children soon became apparent, and the author and his colleagues developed a technique of bronchography suitable even for children as young as 5 months. A suitable dose of barbiturate may be given half an hour before examination, but in children under 2 years, where no local or general anaesthetic is used, the child must be immobilized. A gag is placed in the mouth and, with the index finger of the left hand on the epiglottis or arytenoids as a guide, a No. 12 (French gauge) catheter, mounted on a metallic mandrin previously lubricated by a drop of " lipiodol ", is slipped into the trachea. The mandrin is extracted and the catheter is passed into the required bronchus under screen control. With the child positioned on the cassette, the iodized oil is injected rapidly and the first film taken as the catheter is removed exactly at the end of the injection. The exposure should not be more than one-sixtieth of a second. The lateral film is first taken, and then oblique and anteroposterior exposures in rapid succession. The child rapidly expectorates a large portion of the lipiodol (swallowing most of it) and, if care is taken not to block the small bronchus with the tip of the catheter and inject under pressure, the next day there is hardly a trace of lipiodol in the lung. Altogether 152 patients have been examined without complication.

From a study of this series the author finds that in primary tuberculosis infiltration is the exception, atelectasis the rule. The cause of the collapse may be compression by enlarged lymph nodes or lesions that seem to arise from the bronchial wall itself; the middle lobe is most frequently affected. Distal to the obstruction, bronchial dilatation is the rule and it is surprising to see how rapidly bronchial obstruction may cause irreparable damage to the bronchial tree of a young child. There is wide variation in the type of bronchiectasis, but a tendency to localization in a lobe or segment. A common finding is the " string-bean " appearance, in which the dilated bronchi have circular, incomplete

constrictions at regular intervals; this is considered typical of bronchial obstruction in primary tuberculosis, and occurs with both long-standing and recent lesions. If the obstruction disappears rapidly, the atelectasis also disappears completely and the bronchus almost regains its normal aspect, but chronic atelectasis is thought to be more frequent after primary tuberculosis than is generally admitted.

The article contains reproductions of 14 lateral-view bronchograms. *Sydney J. Hinds*

113. **Diagnosis of Tumors of the Breast by Simple Roentgenography. Calcifications in Carcinomas**

R. LEBORGNE. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 1–11, Jan., 1951. 35 figs., 49 refs.

An account is given of the appearances found in soft-tissue radiographs of tumours of the breast. As a routine the author employs a supero-inferior projection and a low kilovoltage (30 kV or less). The soft-tissue appearances of malignant tumours of the breast and their differentiation from various benign conditions, including fibro-adenomata, cysts, galactoceles, and abscesses, are discussed. Some malignant tumours show fine punctate calcifications which are considered to be characteristic. These may lie within, or partially within, a tumour shadow, or may be seen in the absence of a demonstrable soft-tissue shadow. They can be distinguished from the calcifications to be seen in certain benign conditions, notably fibro-adenomata, which are fewer and coarser and tend to be arranged peripherally, and from those occurring within the lactiferous ducts, which tend to converge towards the nipple. *J. A. Shiers*

114. **The Advantages and Disadvantages of Salpingography with Particular Reference to the Use of Diodone Viscous**

J. H. E. BERGIN. *British Journal of Radiology* [*Brit. J. Radiol.*] **24**, 93–102, Feb., 1951. 11 figs., 16 refs.

A review has been made of 270 cases of salpingography in an attempt to assess the dangers and disadvantages of the method and to ascertain how far these are due to faults in technique and interpretation. At the same time the newer water-soluble media are compared with " lipiodol " in an attempt to assess the value of the former. In 201 cases lipiodol was used and in 69 " viskiosol ". The alleged dangers associated with the use of lipiodol are discussed and the majority are dismissed as being of little consequence. (1) Intravasation. In the present series 3 cases occurred which were thought to be due to trauma of the cervix resulting from instrumental pressure in an attempt to obtain a water-tight joint: they were symptomless. (2) Inspissation. In several of the cases salpingostomy had been performed and the histology was scarcely distinguishable from that of tuberculous salpingitis. Where this happens it is probable that some partial block has previously occurred: it was found only with lipiodol. (3) Infection. Statistical evidence shows that this is twice as frequent with lipiodol salpingography as with insufflation. There is, as yet, no adequate assessment of the frequency of the complication when using viskiosol. Only one case was found in the series which resulted in a moderate pelvic peritonitis. (4) Peritoneal implants. There is no definite evidence that this occurs. (5) Drug reaction. The dangers of this are neither more nor less than in intravenous pyelography. (6) Abortion. Although no figures are quoted it is thought that this is surprisingly rare. Against these possible disadvantages is the rare danger of embolus occurring with kymo-insufflation.

The advantages over insufflation are given as: (1) Determination of the uterine position. A lateral film is advocated for this purpose. Retroversion may be inferred when, on the antero-posterior film, tubal block is present and the uterine cavity remains filled for a considerable period. The cavity also appears elongated. (2) Tubal patency. The exact site of the block can be demonstrated. Two cases of spasm preventing spill are recorded when viskiosol was used, but in both cases it was relaxed by glyceryl trinitrite. It is more common after lipiodol.

In technique the importance of a water-tight joint is emphasized. The injection of the opaque medium under screen control is advocated, and a total of 5 to 6 ml. of lipiodol should be used, or double this amount of viskiosol. A lateral view is followed in 5 minutes by an antero-posterior film to demonstrate delayed spill, loculation, and vaginal reflux.

John H. L. Conway-Hughes

115. **The Roentgen Diagnosis of Upper Abdominal Retroperitoneal Space-occupying Lesions**

A. SHEINMEL and E. A. MEDNICK. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 77–92, Jan., 1951. 7 figs., 8 refs.

The authors describe a modified technique for determining the thickness of the soft tissues behind the stomach, in which the stomach is filled with barium and left lateral erect and right lateral recumbent films are taken instead of the usual supine translateral views. The established technique is considered unsatisfactory because it may fail to show a mass unless it lies in the midline at the point where the stomach crosses the spine, a limited region. It is bound to fail if the mass is on the right side, for the stomach lies almost entirely to the left of the spine in the supine position. The alternative method with the patient prone and the stomach outlined with air instead of barium can be misleading. Appearances simulating a retroperitoneal mass may be produced by ascites, obesity, or even under-inflation of the stomach. With the authors' technique the right lateral recumbent view will show prevertebral tumours, even high ones near the diaphragm, and also many right paraspinal masses, for in this position the cardia and most of the body of the stomach lie in front of the spine, and the antrum and lower body to the right of it. The left lateral erect view will show any masses in the left upper abdomen.

A series of 200 normal subjects were examined to establish the normal appearances. As the depth of the retrogastric space depends on the build, they were classified as hyposthenic, sthenic, or hypersthenic. The

findings in each group are given. It is pointed out, however, that sometimes the presence of a mass may be shown by alteration in the shape of the stomach alone, even though the depth of the retrogastric space remains within normal limits. *J. A. Shiers*

116. **The Radiology of the Intrahepatic Biliary Tract**
M. H. FAINSINGER. *South African Journal of Medical Sciences* [*S. Afr. J. med. Sci.*] **15**, 51–66, Oct., 1950. [received Feb., 1951]. 14 figs., 36 refs.

The intrahepatic biliary tract is frequently outlined during cholangiography, and little modification is required to ensure its regular filling. If a constant pattern can be obtained, deviations from this will be of value in the diagnosis of hepatic tumours, fibrotic lesions, and intrinsic abnormalities of the biliary tract. The author states that the anatomy of the intrahepatic ducts has been inadequately studied, and he describes his attempt to opacify the tract with a suitable injection compound in 35 livers obtained at necropsy. Small pieces of methyl methacrylate plastic were dissolved in acetone to give a strength of approximately 20%, and to this solution 7·5% of bismuth carbonate was added. The injection was performed by means of compressed air at a pressure of 200 mm. Hg. Stereoscopic antero-posterior and oblique views were taken.

The author then describes the normal anatomy of the intrahepatic biliary ducts and some of its variations. He gives the following figures for the normal range of bile-duct diameters: common duct 3 to 8·5 mm.; right hepatic duct 2 to 7 mm.; and left hepatic duct 2 to 6 mm. In cases of tuberculosis with small tubercles, no variation from normal was seen; where the lesions were larger (2 cm.), the ducts were seen in some cases to describe an abrupt curve round them, but without varying in calibre; in the majority, however, the pattern was not affected even by large lesions. In cases of carcinoma the essential features were ductal displacement, areas devoid of ducts, ductal compression, and peripheral ectasia. There was waviness of smaller ducts in one case of portal cirrhosis.

The author also performed cholangiography on 21 patients after cholecystectomy by means of a drainage tube inserted into the common duct at operation. The biliary tract was first irrigated with sterile, warm, normal saline and the mixed bile and saline withdrawn by suction. The tube was then clamped distally and diodone solution injected into it from a 20-ml. syringe through an intravenous needle penetrating the wall of the tube, the injection being controlled by screening. Spot films of the common duct and ampulla of Vater were taken in both the postero-anterior and left anterior oblique positions after about 10 ml. of the contrast medium had been injected slowly; the remaining 10 ml. or less was then rapidly injected, and the exposures repeated in quick succession. If the passage of diodine into the duodenum was not observed on the *x*-ray screen, a film of the area was exposed 15 minutes after injection; if this also was negative 1/100 gr. (0·65 mg.) of glyceryl trinitrate was given sublingually and further films taken after 5 minutes.

Cholangiography in cases of chronic calculous cholecystitis showed that the degree of ectasia varied from minimal to gross, depending on the amount and duration of obstruction. In cases of bilary fistula dilatation was mild and might have been due to cholangitis.

[The author, in describing his method of cholangiography, does not specify the strength of diodone solution used; 50% viscous diodone is the solution employed in most *x*-ray departments in Britain.] *Sydney J. Hinds*

117. **Experimental Neurography**
I. M. TARLOV, D. BERMAN, and J. EPSTEIN. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **64**, 974–988, Dec., 1950. 6 figs., 23 refs.

The authors review the history of research in neurography. They have carried out investigations to find a contrast medium which, when injected into a peripheral nerve, will demonstrate lesions in it, or in the nerve roots, while at the same time producing no functional or anatomical nerve change. The compounds investigated were injected under direct vision into the sciatic nerves of rabbits.

The nerve was elevated by means of a blunt hook. A No. 27-gauge needle, the tip of which had been bent to an angle of 120 degrees, attached to a 1-ml. syringe, was used. It was introduced through the superficial connective tissue and manipulated so that a free flow of medium along the nerve was obtained. Over-distension of the epineural sheath or direct injection into the nerve is undesirable. The injection was made mid-way between the greater trochanter and the popliteal fossa. The opposite nerve was injected with an equal quantity of saline or air. The impairment of motor power was studied by observing the spread reflex of the toes when the suspended animal was suddenly lowered; this disappeared with severance of the nerve. Films were taken immediately after, and sometimes during, the injection. Histological examination was made at necropsy.

The water-soluble compounds were: " argyrol " 50%, " protargol " 15%, " hippuran " 50%, " skiodan " 50 to 100%, " thorotrast " 6·25 to 25%, sodium iodide solution 10 to 100%, " neo-iopax " 25 to 50%, diodone 17·5 to 70%, 6-iodo-D-galactose, " visco-rayopake " 17·5 to 35%. Although with some, visualization was good, their use caused varying degrees of nerve damage as shown by functional tests and microscopically. The dangers of thorotrast from a radiological standpoint are emphasized. The water-insoluble compounds were: iodo-chloral, " lipiodol ", and di-iodotyrosine 25%; all proved too viscous. " Pantopaque ", in amounts of 0·2 ml., produced good visualization and minimal nerve change. This appeared to be the most promising preparation used. When emulsified with " tween 20 ", " tween 80 ", or " yelkin BSS " it became highly toxic to the nerve. Physical emulsions prepared with a supersonic vibrating machine produced good visualization and minimal nerve changes in quantities below 0·2 ml. Insufficient contrast was obtained when air alone was used. *John H. L. Conway-Hughes*

See also Section Hygiene and Public Health, Abstract 14.

Pathology

EXPERIMENTAL PATHOLOGY

118. **Experimental Studies of the Pathogenesis and Morphology of the Crush Syndrome.** (Experimentelle Untersuchungen zur Pathogenese und Morphologie des Crush-Syndroms)
L. KOSLOWSKI. *Zentralblatt für Allgemeine Pathologie und Pathologische Anatomie* [*Zbl. allg. Path. path. Anat.*] **87**, 49–74, Feb. 5, 1951. 12 figs., bibliography.

After an extensive review of the literature the author suggests that the following hypotheses about the crush syndrome can be derived from it: (1) In crushed muscle severe tissue damage results in the liberation of muscle pigment and toxic products of protein breakdown. (2) The circulation is adversely affected by a reduction in blood volume due to the severe oedema of the crushed limb, by the toxic action on capillaries of some of the breakdown products of muscle, and by failure of vasomotor regulation. (3) In the kidney the circulation is at first reduced, and the glomerular filtration is reduced owing to anoxia and low blood chloride level; with re-establishment of glomerular filtration, excretion of muscle pigment and the formation of muscle-pigment and protein casts leads to further epithelial damage and to blocking of the collecting tubules. Death occurs from uraemia.

To test these hypotheses crush syndrome was produced in well-grown healthy rats of 150 to 240 g. weight by clamping the hind limb (or limbs) for about 6 hours with a flat-jawed metal screw-clamp, so that the circulation in the compressed muscle and in the limb distal to it was completely interrupted. If the limb were clamped longer than this, it readily became gangrenous. If both limbs were clamped, the animals died in about 24 hours with evidence of gross circulatory failure; if only one limb was clamped, they usually recovered rapidly from the initial shock and survived more frequently. The tighter the clamp was applied, the more severe the subsequent shock.

Though removal of the clamp led to oliguria (or even anuria), albuminuria, and the presence of erythrocytes and granular casts in the urine, the full crush syndrome as seen in man could not be produced in rats by clamping. Thus although in rats myolysis was severe in the crushed muscle, liberation of myoglobin and consequent myoglobinuria were slight and fleeting. During compression, ischaemia of the renal cortex was marked, but it passed off rapidly when the clamp was removed; the kidney became swollen, and necroses and calcification developed in the first convoluted tubules, but myoglobinaemic nephrosis, anuria due to obstruction of the tubules by myoglobin and protein casts, and uraemia did not occur.

Severe myolysis was produced by intramuscular injection of glycerin or distilled water. In this instance, however, the myoglobinuria was severe but transient; the kidney showed no ischaemia, but a mild glomerulonephrosis without any swelling of the tubular epithelium or myoglobinaemic nephrosis. The renal changes were reversible. The circulatory disturbance was much less and more transient than in compression myolysis, and was never fatal.

The author concludes that the myolysis is due to increase of acids in the compressed musculature, and that the shock is due to absorption of breakdown products of muscle and not to reduction of blood volume, since shock does not occur after glycerin injection. He also considers that neither renal ischaemia nor myoglobinuria alone will produce lower-nephron nephrosis, and that oliguria, aciduria, and low blood chloride level must occur at the same time to lead to nephrosis, anuria, and uraemia. He supposes that myoglobinaemic nephrosis owes its peculiar form to the toxic effect of haematin on the tubular epithelium. *C. L. Oakley*

119. **The Effect of Early Thyroidectomy on the Absorptive Function of the Mesenchymal Tissues.** (Влияние ранней тиреоидэктомии на поглотительную функцию мезенхимы)
M. B. GOLDBERG. Архив Патологии (*Arkh. Patol.*] **12**, No. 6, 57–58, 1950.

Thyroidectomized rats aged 6 to 7 weeks were given trypan blue intraperitoneally. It was found that the absorption of the dye by the reticulo-endothelial system was impaired by comparison with control animals.
L. Crome

120. **Acute Cor Pulmonale. An Experimental Study Utilizing a Special Cardiac Catheter**
C. T. DOTTER and D. S. LUKAS. *American Journal of Physiology* [*Amer. J. Physiol.*] **164**, 254–262, Jan., 1951. 4 figs., 27 refs.

Acute cor pulmonale was produced in 8 dogs (14 experiments), a special radio-opaque cardiac catheter with a thin rubber balloon near the tip being used. The state of acute cor pulmonale was induced by manœuvring the catheter into the left or right branch of the pulmonary artery and then rapidly inflating the balloon so as to obstruct the vessel in which the catheter became lodged. Pulmonary artery obstruction could, of course, be discontinued at will by deflating the balloon. Systolic and diastolic right-ventricular pressures were recorded during the entire period of inflation and at varying intervals following deflation; pulmonary arterial pressures and 3 standard limb leads of the electrocardiogram were simultaneously recorded. The experimental induction of resistance to right-ventricular outflow produced, in all instances, acute right-ventricular hypertension, the average pressure increasing from the control value of 23/2 to 64/8 mm. Hg. In 6 of the 14 experiments right-

ventricular hypertension was maintained for the duration of obstruction, while in the other 8 failure of the right ventricle manifested itself by a continuous rise in the end-diastolic pressures and fall in the systolic pressures with resulting decrease in the pulse pressure. Despite considerable increases above normal in right-ventricular pressure, right axis deviation did not develop.

A. I. Suchett-Kaye

121. **The Effects of Certain Intermediate Products of Metabolism on the Heart.** (Les effets de certains produits du métabolisme intermédiaire sur le cœur)
N. DOBROVOLSKAÏA-ZAVADSKAÏA. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **44**, 35–40, Jan., 1951. 6 figs., 15 refs.

The effect upon the histological appearance of the heart of pyruvic acid and lactic acid was investigated in mice and rats. In the acute cases, dissociation of the myocardial fibres by spaces formerly containing oedematous fluid was found. In the chronic cases, such spaces were invaded by connective tissue which later formed sclerotic plaques. The oedema produced by lactic acid seemed to be more pronounced than that due to pyruvic acid. It was possible to reproduce the clinical picture of beriberi by giving sodium pyruvate alone (without vitamin-B deficiency), whereas this was not the case with calcium or sodium lactate. These findings emphasize the importance of myocardial oedema in conditions of accumulation of pyruvic acid, which is apparently not confined to vitamin-B deficiency. *A. Schott*

122. **Interstitial Myocarditis in Children**
C. G. TEDESCHI and T. D. STEVENSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **244**, 352–357, March 8, 1951. 4 figs., 18 refs.

The authors report 2 cases of interstitial myocarditis in children of 11 months and 6 weeks respectively. The first showed signs of an upper respiratory infection for 26 hours and the second showed gastro-intestinal symptoms for 4 days. In both the pulse was unduly rapid and death occurred rather unexpectedly. In both, also, the heart muscle was flabby but showed no macroscopic lesion. Both hearts showed severe interstitial infiltration by lymphocytes and histiocytes which involved endocardium and epicardium to a minor degree. The lungs showed an interstitial pneumonia. Cultures of heart and lung and also direct examination failed to reveal organisms. From these 2 cases and a study of the literature the authors believe that isolated myocarditis in children is part of a generalized disease of unknown aetiology. *C. V. Harrison*

123. **Pathogenesis of Experimental Arteriosclerosis in Pyridoxine Deficiency. With Notes on Similarities to Human Arteriosclerosis**
J. F. RINEHEART and L. D. GREENBERG. *Archives of Pathology* [*Arch. Path.*] **51**, 12–18, Jan., 1951. 6 refs.

In these experiments rhesus monkeys were subjected to prolonged pyridoxine deficiency. In contrast to the control animals, and to animals suffering from other deficiencies, the pyridoxine-deficient monkeys showed widespread degenerative arterial disease. The main feature was a deposition of excess of a mucopolysaccharide, chiefly in the intima, this being followed by intimal cellular proliferation with formation of fine elastic and collagenous fibrils. The authors suggest that the deficiency causes abnormal protein metabolism, resulting in an excess production of the mucopolysaccharide, which may be the normal ground-substance for the formation of elastic and collagen fibres. In some arteries there was slight increase of mucopolysaccharide in the media. Intimal lipoid deposition occurred only later, and was regarded as a secondary phenomenon; calcification was observed in only one case.

Although admitting some differences, the authors draw a parallel between these changes and those seen in human arteriosclerosis. They maintain, as have earlier workers, that the primary change in arteriosclerosis is a gelatinous swelling of the intima and that fat and cholesterol appear secondarily. In addition the authors postulate that mucopolysaccharide may have a special affinity for lipoids and suggest that this aspect of the subject be investigated further, together with any relationship that pyridoxine may have to human arteriosclerosis. *G. J. Cunningham*

124. **The Constriction Tolerance and Critical Threshold of Constriction of the Coronary Vessels.** (Über die Drosselungs-toleranz and die kritische Drosselungsgrenze der Herz-Coronargefässe)
H. REIN. *Pflügers Archiv für die Gesamte Physiologie* [*Pflüg. Arch. ges. Physiol*] **253**, 205–223, 1951. 8 figs., 17 refs.

Carefully controlled experiments were carried out on 19 dogs. The animals were anaesthetized with intramuscular "pernocton", the author pointing out the inadvisability of using intravenous barbiturates for experiments on the heart. At operation, a "stereotaxic" precision screw was put around one of the coronary arteries, and the pericardium and thorax closed again. The screw could be operated from outside the thorax, and blood flow distal to the occlusion was measured with Rein's diathermy *thermostromuhr* (*Ergebn. Physiol.*, 1944, **45**, 514). The pressure in the aorta and right atrium was also recorded. Artificial respiration was maintained throughout, controlled so as to keep the carbon dioxide content of the expired air within normal limits.

Rapid constriction (of varying degrees of severity) of the right coronary artery gave rise to an immediate "compensatory vasodilatation" in the region distal to the block. If the constriction was of short duration, such as 0·1 minute, unclamping of the artery was followed by a reactive hyperaemia during which the blood flow might reach 200% of its resting value. Unless the constriction amounted to complete obliteration, no signs of cardiac insufficiency (as judged by a rise in right atrial pressure and a fall in aortic pressure) appeared. If constriction was maintained for a longer time (0·3 minute), another factor came into operation in the opening-up of arterial collaterals from regions of the myocardium supplied by the posterior left coronary artery. This

increased blood supply to the area beyond the block made the immediate local compensatory vasodilatation superfluous and it disappeared, so that when the screw was released in such a case there was little or no sign of reactive hyperaemia. During severe and long-lasting constriction of the right coronary artery, signs of failure of the whole myocardium might appear. It is suggested that this generalized failure was due to blood being drained off in excess from the region supplied by the left coronary arteries to the ischaemic area beyond the block.

On occasion a third factor made its appearance. In some experiments signs of cardiac insufficiency began to develop during a severe constriction, at a time when the collaterals must already have opened up; then these signs disappeared again and the heart action returned to normal before the constriction was released. This was not accompanied by any change in flow distal to the block. Two possible explanations are offered: in relative ischaemia the heart muscle may for a short time revert to a metabolism that makes a lower oxygen demand than normal; or arterio-venous anastomoses, demonstrated histologically by Hirsch (*Cardiologia, Basel*, 1942, **6**, 31), situated beyond the point of measurement of blood flow and normally open, may under the influence of hypoxia close down, providing additional blood for the hypoxic muscle.

The exact nature of the stimulus that calls forth these compensatory changes is not known. The changes are independent of the extrinsic nerves of the heart and are unlikely to be dependent on intrinsic " pressor receptors " in the coronaries. Oxygen lack is almost certainly involved; this is borne out by the findings of American workers using Kety and Schmidt's [more reliable] nitrous oxide method of measuring coronary blood flow.

These results draw attention to the adaptability of the coronary circulation under conditions as nearly normal as possible. The older " mechanistic " view of the absolute dependence of coronary flow on arterial pressure was largely a product of highly artificial experimental conditions such as were imposed by Starling's or Langendorff's preparations. As with other muscular organs, the " constriction tolerance ", that is, the amount of passive mechanical constriction of a blood vessel possible before the region distal to the block shows compensatory reactions, is almost *nil*; the " critical threshold of constriction ", the point at which the compensatory reactions become insufficient and the organ begins to fail, can in the case of the coronaries rise surprisingly high, at any rate for a short time, if the heart is in a good condition. *P. Mestitz*

125. **Coronary Insufficiency and Arterial Hypertension.** (Коронарная недостаточность и артериальная гипертония)
M. A. Volin, E. E. Tsvilikhovskaya, T. E. Beslekoyev, and V. S. Mayat. Терапевтический Архив [*Terap. Arkh.*] **22**, No. 6, 17–25, 1950. 11 figs.

The authors, in a series of experiments on 7 dogs, found that ligation of a branch of the coronary artery resulted in hypertension. The electrocardiographic changes were those typical of cardiac ischaemia. The dogs were killed from 1½ to 2 years after operation, and necropsy performed. Histological studies revealed hypertrophy of the ventricular heart muscle, and in some cases the kidneys showed sclerotic changes.

The authors regard this experimentally produced hypertension as being due to reflex stimulation of the vasomotor centres, associated with irritation of the receptors of the coronary vessels and heart-muscle by products of disturbed metabolism from anoxia. They suggest that a similar mechanism may operate in clinical coronary ischaemia. *L. Firman-Edwards*

126. **The Development of Lymphatic and Myelogenous Leukemia in Wistar Rats following Gastric Instillation of Methylcholanthrene**
H. Shay, M. Gruenstein, H. E. Marx, and L. Glazer. *Cancer Research* [*Cancer Res.*] **7**, 29–34, Jan., 1951. 24 refs.

Spontaneous leukaemia in rats is extremely rare and has not been recorded in the Wistar strain. In only one instance has leukaemia been induced. The authors have observed 8 cases of leukaemia in a total of 59 Wistar rats (not inbred) to which methylcholanthrene had been administered by stomach tube for 1 to 14 months. Six of the cases were of the lymphatic and 2 of the myelogenous type. One animal with induced lymphatic leukaemia was killed and a suspension of the spleen injected intraperitoneally into 3 other rats, 2 of which subsequently also showed a lymphoblastic blood picture and histological signs of leukaemia.
J. F. Loutit

127. **Experimental Leucopenia in the Rat and its Treatment with Vitamins, Heavy Metals, and Other Agents.** (Experimentelle Leukopenie der Ratte und ihre therapeutische Beeinflussung durch Vitamine, Schwermetalle und andere Wirkstoffe)
R. Jürgens and A. Studer. *Acta Haematologica* [*Acta haemat., Basel*] **5**, 47–64, Jan., 1951. 4 figs., 20 refs.

A synthetic diet to which 1% succinylsulphathiazole was added was given to 1,000 rats, 351 of which developed folic acid deficiency and therefore granulocytopenia, mainly after 4 or 5 weeks. Segmented neutrophils were affected most markedly. Induced leucopenia does not remit spontaneously in rats, but progresses. The addition of 10 μg. of folic acid, however, caused a rise in leucocyte count, which was not much greater with higher doses. With diet and succinylsulphathiazole the weight of rats increased steadily at first, but when leucopenia developed there was no further gain, and later they lost weight. Folic acid caused resumption of a steady gain in weight. Two doses of folic acid maintained leucocyte counts at normal levels for about 3 weeks. Folic acid also acted well when leucopenia had been made more severe by nitrogen mustard. Small doses of folic acid antagonists, such as methyl- or dimethyl-folic acid, given simultaneously with folic acid did not inhibit its effect on leucocyte count, but large doses caused a further fall. Vitamin A, ascorbic acid, and iron stimulated leucopoiesis, but ribo-

flavin, vitamins B_6 and B_{12}, α-tocopherol, nucleic acid derivatives, cobalt nitrate, nickel acetate, methionine, and tyrosine did not. *E. Neumark*

128. **The Action of Collagenase on Skin and the Anti-collagenase Factor in Human Serum**
R. B. STOUGHTON and A. L. LORINCZ. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **16**, 43–52, Jan., 1951. 2 figs., 13 refs.

Collagenase activity on human skin *in vitro* was investigated. [For details of the methods employed the original paper should be consulted.] Filtrates of *Clostridium welchii* Type A were used as a source of collagenase. Such filtrates, containing also hyaluronidase, lecithinase, and the theta-toxin, attack the polysaccharide component of acetone-fixed skin, leaving morphologically intact collagen bundles and elastic fibres. The authors describe a method of estimating the collagenase activity of the filtrate quantitatively. They found that normal human serum albumin, unlike globulin, has an anti-collagenase activity and that the serum of 3 patients with lupus erythematosus and of one with dermatomyositis showed a decreased anti-collagenase activity. *S. T. Anning*

129. **The Agglutinating Factor for Sensitized Sheep Erythrocytes in Serum and Joint Fluid from Rheumatoid Arthritis Patients**
N. SVARTZ and K. SCHLOSSMANN. *Annals of Rheumatic Diseases* [*Ann. rheum. Dis.*] **9**, 377–379, Dec., 1950. 4 refs.

130. **The Sequence of Changes in the Histamine and Histaminase Content of the Lungs and Blood of Rats During the Early Stages of Experimental Silicosis.** (Динамика изменений гистамина и гистаминазы в легких и крови у крыс на ранних стадях экспериментального силикоза)
V. I. USPENSKY. Архив Патологии [*Arkh. Patol.*] **12**, No. 6, 26–30, 1950. 4 figs., 8 refs.

The histamine content and the histaminase activity of the lungs and blood were estimated biologically at various intervals after the intratracheal introduction of sodium silicate. After the first few hours and days the histamine content of the lungs fell and the histaminase activity increased both in the lungs and in the blood. Later, the histamine content of the lungs rose along with the development of silicosis, while the histaminase activity fell. This accumulation of histamine in the lungs is possibly the result of the toxic action of silicic acid and may be one of the pathogenetic factors in the subsequent development of the fibrosis in the lungs.
L. Crome

131. **Aetiology of Chronic Gastric Ulcer. Observations on the Blood-supply of the Human Gastric Mucosa with a Note on the Arteriovenous Shunt**
F. S. A. DORAN. *Lancet* [*Lancet*] **1**, 199–202, Jan. 27, 1951. 6 figs., 49 refs.

Virchow's hypothesis that chronic peptic ulcer is due to infarction of a part of the mucosa has lost support in recent years, since it has never been possible to produce chronic ulceration through infarction alone. The author feels that a modified vascular hypothesis could still be of value in helping to explain the situation of a chronic peptic ulcer, especially in the stomach. The technique employed in the investigation was to inject a suitable artery in a portion of stomach recently removed, usually within the hour. Injection was with 10% silver iodide. Leakage was prevented by ligation of all points. The specimen was then radiographed to confirm that filling of the arterial system was complete, the stomach being slit open and radiographed when flat. Four specimens used to demonstrate the arterio-venous shunt were treated by the haematoxylin method of Grant. Previous accounts of the vessels supplying the mucosae were confirmed. There is an anastomosis between the mucosal vessels and those in the muscularis mucosae, from which branches arise, piercing the mucosa to reach the subepithelial layer. These vessels in turn form an anastomosis in the substance of the mucosa. Several specimens showed that the lesser curvature has fewer vessels per unit area of mucosal surface than has the greater curvature. It is interesting to note that in cases of duodenal ulcer the density of vessels seemed to be the same on both curvatures.

If in addition to a decreased vascularity the blood supply could further be diminished by an arterio-venous shunt of blood in the submucosa, there might be some support for the view that vascularity played a part in the production of ulcer. The arterio-venous shunts previously described are said to be opened by sympathetic action. Thus in stomachs removed after general anaesthesia, where the sympathetic had not been blocked, injection material did not enter the mucosa. In resections where spinal block had been used, the injection material reached the mucosa since the shunt had not been operating. These findings were not confirmed. In addition, the number of shunts did not appear to be large enough to cause extensive diversion of blood from the mucosa and there was also no evidence that any injection material passed back up the valveless veins into the mucosa. The author concludes that the lower vascular density of the lesser curvature is probably a factor in localizing ulcers in this region, and the aetiological significance which has been attributed to the arterio-venous shunt is premature. Sixteen stomachs were examined. *J. G. Jamieson*

132. **Role of Somatotrophic Hormone in the Production of Malignant Nephrosclerosis, Periarteritis Nodosa, and Hypertensive Disease**
H. SELYE. *British Medical Journal* [*Brit. med. J.*] **1**, 263–270, Feb. 10, 1951. 12 figs., 20 refs.

Female rats treated with electrophoretically pure somatotrophic hormone (STH) develop polyuria and hypertension, with nephrosclerosis, myocarditis, and pancreatic polyarteritis nodosa. The liability of the animals to these toxic effects is augmented by unilateral nephrectomy and an excessive intake of sodium chloride. The toxic effects are similar to those produced previously by treatment with high doses of deoxycortone acetate (DCA) or a mixed anterior pituitary hormone

preparation (LAP) which is rich in growth factor. They can be prevented by giving cortisone simultaneously in big enough doses to produce adrenal cortical atrophy. STH also increases the liability of rats to experimental arthritis, while simultaneous administration of cortisone inhibits it, but larger doses of cortisone are required to prevent arthritis in STH-treated than in untreated rats.

It is suggested that STH stimulates the production of mineralo-corticoids like DCA by the adrenal cortex and also sensitizes the peripheral tissues to DCA-like substances. STH appears to be as important as ACTH in the production of the " diseases of adaptation ". It is responsible for the activity of the mineralocorticoids which stimulate defensive granuloma formation, while ACTH is responsible for the activity of the glucocorticoids which inhibit such defensive mechanisms.

A. C. Crooke

133. **Studies on Salt Hypertension. Effects of Adrenalectomy and Nephrectomy**

W. L. Brandt, W. M. Dubin, and L. A. Sapirstein. *American Journal of Physiology* [*Amer. J. Physiol.*] **164**, 73–78, Jan., 1951. 3 figs., 11 refs.

Instead of drinking water, 20 rats were given a 2% sodium chloride solution and all developed hypertension and cardiac hypertrophy at the end of 6 weeks. The animals were then separated into two groups of 12 and 8, the first being subjected to bilateral adrenalectomy and the second to an equivalent operation in which the adrenals were manipulated but not removed. After the operation the rats continued on sodium chloride and, at the end of 4 weeks, it was noted that the blood pressure both in sham-adrenalectomized controls and in adrenalectomized animals remained at comparably high levels. It is concluded that salt hypertension, once established, persists in spite of total adrenalectomy. Furthermore, in the adrenalectomized rats cardiac hypertrophy disappeared despite the persistence of hypertension. In other experiments it was shown that salt hypertension is a reversible process and can be made to disappear by replacing sodium chloride with tap water. In a group of 7 salt-induced hypertensive rats, bilateral nephrectomy was performed. The hypertension persisted as long (about 3 days) as the animals survived.

It appears that salt hypertension in rats is not mediated through the adrenal gland or kidney.

A. I. Suchett-Kaye

134. **Histologic and Perfusion Studies of the Unmanipulated Kidney in Rabbits with Unilateral Renal Hypertension**

J. Flasher, H. A. Edmondson, and D. R. Drury. *Archives of Pathology* [*Arch. Path.*] **51**, 53–67, Jan., 1951. 5 figs., 29 refs.

Clamping the renal artery of one kidney produces hypertension. In rabbits, this hypertension lasts longer than in dogs, in which it may last for only a few weeks. Removal of the manipulated kidney in dogs brings the pressure back to normal immediately. In the present experiment with rabbits removal of the manipulated kidney brought the pressure to normal in half the animals, but in the other half the hypertension persisted. No reason for this persistence was found in the normal kidney either on histological examination or on perfusion with 5% gelatin in normal saline. A high incidence of renal scarring, presumably due to staphylococcal infection, was noted in all animals which had been operated upon.

D. M. Pryce

135. **Diffuse Glomerulonephritis Induced in Rabbits by Small Intravenous Injections of Horse Serum**

C. R. McLean, J. D. L. Fitzgerald, O. Z. Younghusband, and J. D. Hamilton. *Archives of Pathology* [*Arch. Path.*] **51**, 1–11, Jan., 1951. 3 figs., 22 refs.

Diffuse glomerulonephritis developed in 20 of 31 rabbits receiving daily 0·5-ml. injections of horse serum for periods up to 13 months. The process was associated with the development of precipitins. Two animals did not develop precipitins or nephritis. Two animals had precipitins and nephritis but were negative to monthly skin tests.

The glomerulonephritis produced by large doses of foreign serum is frequently accompanied by arteritis and endocarditis, but these phenomena were absent in the present experiment. The histological changes were of acute, subacute, and chronic types and in the late stages were associated with nitrogen retention.

To enhance the effects of the injections unilateral nephrectomy was performed at various stages in 20 animals.

D. M. Pryce

136. **The Effect of Ascorbic Acid on the Protein Metabolism in Experimental Damage of the Liver.** (Влияние аскорбиновой кислоты на белково-азотистый обмен при экспериментальных поражениях печени)

Z. M. Volinski. Архив Патологии [*Arkh. Patol.*] **12**, No. 6, 30–34, 1950. 4 figs., 15 refs.

The liver was damaged in rabbits by the continued administration of carbon tetrachloride, and the functional effect of the resulting liver damage assessed by means of the measurement of the amino-acids in the urine and by the degree of polipeptidaemia. One-half of the animals were given ascorbic acid. It was found that liver damage was less severe and persistent in those animals which had received the ascorbic acid.

L. Crome

137. **Isolation of a Filtrable Virus from a Hydatidiform Mole Undergoing Chorionepitheliomatous Change.** (Isolement d'un virus filtrable dans une môle hydatiforme en voie de transformation chorio-épithéliomateuse)

R. De Ruyk. *Bulletin de l'Association Française pour l'Étude du Cancer* [*Bull. Ass. franç. Cancer*] **38**, 52–71, 1951. 15 figs., 1 ref.

The author, working at the Institut de Recherches sur le Cancer, Gustave-Roussy, claims to have obtained an agent from 2 cases of human hydatidiform-mole tissue capable of producing proliferative lesions in the membranes of developing eggs. A piece of mole tissue was obtained by uterine curettage. Histological examination established the diagnosis of hydatidiform mole with

chorionepitheliomatous change. An extract of the tissue was passed through a Seitz filter and injected into the chorio-allantois (C-A) and the amniotic cavity of 8- to 12-day chick embryos. Proliferative lesions of all three layers of the C-A and of the amnion developed. [With the possible exception of the ectodermal lesion of the C-A, these are not sufficiently different from non-specific lesions to carry conviction.] Similar lesions were produced by a second passage in eggs, but no further passage appears to have been possible. Extracts of the original and of egg-passage material, purified by differential centrifugation, were examined in the electron microscope. Fairly uniform spherical particles of about 100 mμ diameter were found. [Here also the possibility that these were of non-specific origin was not excluded.]

M. H. Salaman

MORBID ANATOMY

138. The Edendale Joined Twins

L. R. TIBBIT. *South African Medical Journal* [*S. Afr. med. J.*] **25**, 17–20, Jan. 13, 1951. 5 figs., 3 refs.

Few necropsies on joined twins are reported in the literature, although there are numerous descriptions of the external appearance of such joined twins. The birth of female joined twins in August, 1949, in South Africa apparently presented no particular difficulty and they made excellent progress until half-way through their fifth month. Then a severe cough started in the left twin, followed by fever and gastro-enteritis in both. On the third day of illness the respiration of the left twin ceased. The right twin died 10 minutes after the left.

At necropsy the following findings were recorded. The weight was 11 lb. 2 oz. (5 kg.). The heads, necks, arms, and chests were those of two separate babies showing signs of marked dehydration, These parts were facing each other. The twins were joined from the costal margins downwards and appeared to have one pelvic girdle between them, with two normal " anterior " legs, except that the right showed a marked degree of talipes equino-varus. Attached to the posterior part of the pelvic girdle was a larger " third leg " with a thicker calf and thigh. This third leg was a partially duplicated lower limb, presenting a double foot with a total of nine toes, the big toe remaining fused. There was a single umbilicus slightly to the right of the midline of the common abdominal wall.

There were two sets of external genitalia in the perineum, with one anus between these two genitalia. The anterior genitalia consisted of two labia majora and minora, with the urethra in the usual position in the vestibule. Lying posterior to that was a vagina traversed by a septum running longitudinally. The posterior genitalia consisted of a vagina anteriorly, behind which there was a dimple only in the place of the urethral opening, surrounded by labia minora only. There appeared to be no abnormalities in the cranial cavities. Each twin had a separate central nervous system and a complete vertebral column, including a separate sacrum and coccyx. Both pairs of lungs and both hearts appeared anatomically normal and equal in size. The left lung of the left twin showed an advanced broncho-pneumonia. Each aorta was normal. The diaphragm was obviously double in structure, with four crura. The single abdominal cavity contained one large liver, obviously a double structure, with two gall-bladders; dissection showed that there had been a ductus venosum for each twin. There was duplication of the spleen, oesophagus, stomach, bile ducts, pancreas, duodenum, and jejunum. The ileum of each twin joined a common caecum with one vermiform appendix. There was a single large intestine and anus.

Each twin had a set of two hip bones and a sacrum. The anterior part of the girdle consisted of normal-shaped pubic rami joined at the pubic symphysis, except that one " anterior " hip bone from each twin entered into the joint. The two " posterior " hip bones, one from each twin, fused into a spindle-shaped mass of bone posteriorly. The acetabulum for the single hip-joint of the third leg was seen on the outer aspect of this spindle of bone. The contents of the common pelvic cavity, from before backwards, were an " anterior " bladder, uterus, and appendages, a rectum, and a " posterior " bladder, uterus, and appendages. There were two " anterior " large kidneys (one from each twin) with two corresponding normal ureters running into the " anterior " bladder and urethra. There were two very small " posterior " kidneys with large, dilated, convoluted ureters running into a large flattened bladder situated retroperitoneally against the spindle of bone. The ureteric orifices of this bladder were large. There was a dimple at the anterior angle of the trigone where the urethral orifice should have been. The " anterior " uterus was normal, with normal appendages. The " posterior " uterus lay to the left of the " posterior " bladder, broad at the base and tapering into a partially bicornuate fundus. There were small " posterior " ovaries.

The various theories of the causes and mechanism of twinning are discussed. *Lilian Raftery*

139. Heterotopic Glial Nests in the Subarachnoid Space: Histopathologic Characteristics, Mode of Origin and Relation to Meningeal Gliomas

I. S. COOPER and J. W. KERNOHAN. *Journal of Neuropathology and Experimental Neurology* [*J. Neuropath. exp. Neurol.*] **10**, 16–29, Jan., 1951. 13 figs., 23 refs.

Small islands, nests, or peninsulas of glial tissue may be present within the subarachnoid space of human subjects. The occurrence of these nests has been called " glial heterotopia ". These heterotopic structures are rarely observable grossly as small tubercle-like granules over the leptomeninges. More commonly, however, the presence of heterotopic glial tissue in the subarachnoid space results in an opaque thickening of the leptomeninges, very often simulating a picture of a chronic adhesive arachnoiditis. In approximately 80% of cases the presence of subarachnoid heterotopic glial tissue cannot be detected by gross examination of the nervous system. The most frequent site of occurrence of subarachnoid heterotopic glial tissues is at the level of the

medulla oblongata. The second most commonly affected site is at the lumbosacral level of the spinal cord.

Neurological nests were found to demonstrate four distinct architectural patterns, the most common being that originally reported by Wolbach. This type consists of a glial island enclosed in a pial sheath. Astrocytic nuclei are grouped centrally and the circumferential glial fibers run isomorphically in an arched manner similar to that of the subpial marginal glia of the spinal cord.

Subarachnoid heterotopic glial structures are formed by the protrusion of mature glia from the neuraxis. In some instances these glial protrusions are " pinched off " and come to lie free in the subarachnoid space or, rarely, in the extraspinal tissues.—[Authors' summary.]

140. **Non-lipoid Histiocytic Reticulosis with Meningioma Interrupting Pituitary Stalk**
T. L. LINN. *American Journal of Clinical Pathology* [*Amer. J. Clin. Path.*] **21**, 123–132, Feb., 1951. 12 figs., 13 refs.

A woman of 43 suddenly developed excessive thirst and polyuria, and the diagnosis of diabetes insipidus was made. She was treated with 1 ml. " pitressin " tannate in oil every 3 days initially, but in the course of the next 5 years the dose was increased to 1 ml. daily. By this time she had developed a painful swelling below the angle of the right mandible and areas of osteolysis were noted on *x*-ray examination of the skull, ribs, femora, pelvic bones, and vertebrae. Appearances in biopsy material obtained from an enlarged lymph node and a rib were consistent with eosinophilic granuloma. About a year later *x*-ray examination of the chest showed fibrotic markings in both lungs, gradually becoming more prominent. At the same time there was continued extension of osteolysis throughout the skeleton, and hepatomegaly, splenomegaly, and pyrexia developed in the last month of life. The patient died 7 years after the onset of the illness.

At necropsy, both lungs showed coarse " honeycomb " fibrosis. There was generalized enlargement of the lymph nodes and both the liver and spleen were enlarged. There were numerous foci of yellow, gelatinous, haemorrhagic tissue in the verebral marrow, and excavated areas in the skull bones contained similar tissue. An irregular plaque of soft, white tissue was found lying upon the dorsum sellae near its right side. The base of the sella turcica appeared intact and the pituitary itself showed no gross abnormality. The stalk, however, was twice the normal thickness, with associated thickening of its dural investment. Similar nodules of tissue were present in the anterior and middle fossae.

Microscopical examination showed the lesions over the dorsum sellae and adjacent areas to be meningiomatous. The tumour was closely applied to the pituitary capsule and invaded the stalk. The lesions in the other parts of the body showed a histiocytic reticulosis, the picture being that of a histiocytic proliferation with giant-cell formation and occasional eosinophils. Often there was necrosis and a dense neutrophil infiltration. No histiocytic involvement of the pituitary was found, so that the meningioma had here produced a complication commonly ascribed to the " granulomatous " process. The author suggests that if the arachnoid cells be regarded as part of the reticulo-endothelial system, capable of occasional response in reticulo-endothelial cell proliferation involving other body areas, the occurrence of multiple meningiomata in this case is possibly related to the reticulosis and does not represent a coincidental and separate condition. *R. B. Lucas*

141. **The Initial Stages in Post-operative Pneumonias.** (О начальных изменениях при послеоперационных пневмониях)
B. O. PRESS. Архив Патологии [*Arkh. Patol.*] **12**, No. 6, 41–43, 1950. 3 refs.

The lungs of 30 patients dying soon after operation were studied radiologically and histologically. The earliest microscopic changes consisted invariably of the transudation of blood from the capillaries into the alveolar space. Atelectasis did not appear to play a major part in the pathogenesis of the condition.
L. Crome

142. **Abscess Formation in Myocardial Infarction**
C. G. TEDESCHI, T. D. STEVENSON, and H. M. LEVENSON. *New England Journal of Medicine* [*New Engl. J. Med.*] **243**, 1025–1027, Dec. 28, 1950. 3 figs., 7 refs.

Two cases of abscess formation in myocardial infarction are described. A woman of 69 died on the 7th day after a posterior basal myocardial infarct due to thrombosis of the main right coronary. The infarct contained pin-point abscesses and had ruptured, producing tamponade. Coagulase-positive staphylococci were cultured from the abscesses and from accompanying lesions of bronchopneumonia. A man of 75 died on the 4th day after an anterior apical infarct. This contained similar pin-point abscesses, and coagulase-positive staphylococci were isolated from the abscesses and from bronchopneumonic lesions.

The authors suggest that a bacteriaemia arose from the pneumonia and the cocci settled in the necrotic muscle. They claim that only one case has previously been recorded. *C. V. Harrison*

143. **Arteritis of Striated Muscle in Rheumatoid Arthritis**
L. SOKOLOFF, S. L. WILENS, and J. J. BUNIM. *American Journal of Pathology* [*Amer. J. Path.*] **27**, 157–173, Jan.–Feb., 1951. 9 figs., 10 refs.

Biopsy of striated muscle revealed an arteritis in 5 out of 57 cases of rheumatoid arthritis. The lesion was not directly connected with the affected joints, as the portions of muscle sectioned were taken at areas remote from them. A specific lesion is thought to have been found in view of the constancy of its anatomical location and because similar lesions were not encountered in other conditions. The vessels involved were large arterioles or small arteries. The histological features were not distinctive, and consisted of a granulomatous inflammation which might be localized in the adventitia or extend through all three arterial coats. Neither endothelial destruction nor collagenous necrosis was seen,

and thrombosis did not occur. In a discussion of the lesion a useful comparative table is given, showing the main differences in several types of arteritis.

[It is unlikely that this lesion will be of diagnostic value in view of its infrequency and the fact that only a few of a large number of serial sections showed the histological changes. This probably accounts for the negative findings of earlier workers.]

G. J. Cunningham

144. **Pathological Changes in the Nerves and their Endings in Striated Muscles in Purulent Lesions Combined with General Septic or Toxic Phenomena.** (Патологические изменения внутримышечных нервных стволов и их окончаний в поперечнополосатой мускулатуре при гнойных процессах с общими септическими или токсическими явлениями)

U. M. Zhabotinsky. Архив Патологии [*Arkh. patol.*] **12**, No. 6, 15–19, 1950. 4 figs., 5 refs.

Nerve lesions were studied histologically in striated muscle taken from 20 subjects dying from septicaemia. Degenerative and, sometimes, regenerative changes were found in all of them and these were not confined to sites in the vicinity of the infection. The muscle fibres themselves were not usually involved. The nerve changes are described in detail. Both the main nerves and their end organs, motor and sensory, were involved.

L. Crome

145. **Hodgkin's Disease and Hodgkin's Sarcoma: with Report of a Case in which Both Conditions were Present Simultaneously**

R. I. S. Dunn. *Glasgow Medical Journal* [*Glasg. med. J.*] **32**, 31–41, Feb., 1951. 6 figs., 42 refs.

The author discusses the unitarian view of the histogenesis of the various kinds of tumours of lymphoid tissue and describes a case of sarcomatous Hodgkin's disease.

R. A. Willis

146. **Lipophage Granuloma of the Subcutaneous Fatty Tissue (Injection Granuloma).** (Lipophage Granulome im Unterhautfettgewebe. (Injektions-Granulome))

M. Buser. *Schweizerische Medizinische Wochenschrift* [*Schweiz. med. Wschr.*] **80**, 1361–1365, Dec. 23, 1950. 3 figs., 25 refs.

A series is described of 21 cases of subcutaneous granuloma, of which 19 occurred in women and most of which developed several months or years (up to 25) after injection of medicaments in oily suspension. Clinically, the lesion was a firm, frequently tender, subcutaneous nodule. On excision, this appeared to consist of fatty tissue traversed by fibrous bands and incorporating a varying number of tiny cysts. Microscopically, the latter proved to contain oily substances. They were surrounded by lipophages and numbers of foreign-body giant cells; later ordinary granulation tissue was seen, many cells also containing fat droplets. In some cases the granulation tissue was of a nodular, tuberculoid structure, and in these an increase of reticulum fibres was demonstrable. Birefractile crystals were embodied in giant cells, and iron-containing macrophages were occasionally numerous. The older the lesion, the greater the tendency to fibrosis. Three stages in the development of the lesion are recognized. An initial fat necrosis (due to toxic, traumatic, or ischaemic factors), followed by a short exudative phase which in most cases, and especially where the lesion is small, heals without scarring, but is occasionally followed by the granulomatous phase, where the insoluble or almost insoluble substances are encapsulated.

[Too little emphasis is placed on the part played by the substances injected.]

R. Salm

147. **Unilateral Renal Cortical Necrosis and Unilateral Benign and Malignant Nephrosclerosis Associated with Contralateral Artery Occlusion: Report of a Case**

S. M. Aronson and M. C. Sampson. *Archives of Pathology* [*Arch. Path.*] **51**, 30–37, Jan., 1951. 3 figs., 15 refs.

The case is described of a man of 52 who complained of cough, fever, headache, and loss of weight. At necropsy the left kidney showed the changes of benign and malignant hypertension and gross cortical necrosis. The right kidney was normal. The renal artery on the right side was grossly sclerotic, with marked reduction of the lumen, which was terminally thrombosed. There were old and recent infarcts in the heart, a non-tuberculous cavity in the lung, and [?] viral hepatitis. The pituitary gland was normal.

It is thought that the hypertension was due to ischaemia of the right kidney, and that this was unaffected by the cortical necrosis because its functional activity was low and its nutritional demands adequately supplied by the capsular anastomotic vessels.

D. M. Pryce

CLINICAL PATHOLOGY

148. **The Quantitative Leucocyte Index during the Course of Infections Treated with Penicillin.** (L'évolution des infections traitées par la pénicilline et l'indice quantitatif des leucocytes)

E. Szczeklik, T. Kochmánski, and W. Dwernicka. *Sang* [*Sang*] **22**, 42–56, 1951. 4 figs., 4 refs.

During the treatment of infections with penicillin, granulocytes decrease, while the percentage of non-granular leucocytes (monocytes and lymphocytes) increases as improvement occurs; the opposite condition develops if penicillin fails. The authors therefore regard the ratio of granulocytes to agranulocytes, the average normal value of which is in the region of 2·5, as of great prognostic value, and support their conclusions by the study of 70 cases.

A. Piney

149. **Rapid and Simple Method of Estimating Haemoglobin**

G. K. Welch and W. W. Walther. *Lancet* [*Lancet*] **1**, 548–549, March 10, 1951. 6 refs.

The authors describe a method of estimating haemoglobin which they have used for some years and for which they claim the advantages of speed, accuracy,

stability, and simplicity. The pigment used is oxyhaemoglobin, 20 c.mm. of blood being diluted with 1% ammonia and its colour measured in a single-celled absorptiometer, the tube of which has been so calibrated that the scale reading of the instrument represents half the haemoglobin percentage.

With these calibrated tubes time is saved in measuring the diluent and the tubes need not be dried between estimations. Variation in the bore of the tubes is also overcome by this initial calibration. [The method is certainly simple and quick, but the tables illustrating its accuracy with various lights and in comparison with an alkaline-haematin method are based on tests performed on one sample of blood only, which probably accounts for the very accurate agreement. Nevertheless, the method would appear to be very useful in laboratories where large numbers of estimations are done by several different, and often junior, workers.]

R. F. Jennison

150. **Antihyaluronidase Content of Serum in Children Suffering from Hemolytic Streptococcal Infections, Rheumatic Fever and Other Diseases.** [In English]
M. R. H. Stoppelman. *Acta Paediatrica* [*Acta paediatr., Stockh.*] **39**, 510–523, 1950. 1 fig., 7 refs.

The serum antihyaluronidase level was determined in 705 children by the mucin-clot prevention method of Quinn. There were considerable variations in healthy children, but on average the titre increased with age. The estimation was carried out on 11 children with active rheumatic fever and in 10 of these high titres were found, but in only 3 cases was the titre above the highest found in healthy children. The author concludes that the test may give useful confirmatory evidence in the diagnosis of rheumatic fever, but that it is certainly not diagnostic of the condition. It seems that the titre fell when the activity subsided, or when chemoprophylaxis was given. *R. S. Illingworth*

151. **Variation and Error in Eosinophil Counts of Blood and Bone Marrow**
W. R. Best and M. Samter. *Blood* [*Blood*] **6**, 61–74, Jan., 1951. 10 figs., 35 refs.

The sources of error inherent in the chamber eosinophil count are described: 99% of observations in 143 successive clinical determinations were found to lie within the expected limits as calculated from the formula. The theoretical limits of chance variation in differential eosinophil counts in marrow smears were calculated with the *chi*-square formula, but the observed error exceeded this estimate, a finding attributed to clumping of eosinophils. Peripheral eosinopenia induced by adrenocorticotrophin (ACTH) was not accompanied by any significant change in marrow eosinophils.

The physiological variations in eosinophil counts are reviewed. Serial counts show a significant diurnal variation with considerable minute-to-minute fluctuations superimposed upon it; 38% of normal subjects had a maximum morning fall of eosinophils of at least 50%. A single eosinopenic response to ACTH or adrenaline is not an unequivocal test for the integrity of the hypothalamus–pituitary–adrenal chain, and repeated and controlled observations are necessary. Ephedrine was as effective an eosinopenic agent as adrenaline.

P. C. Reynell

152. **The Normal Megakaryocyte Concentration in Aspirated Human Bone Marrow**
F. G. Ebaugh and R. M. Bird. *Blood* [*Blood*] **6**, 75–80, Jan., 1951. 2 figs., 8 refs.

The authors describe a chamber method for counting megakaryocytes in aspirated sternal marrow. The diluting fluid was Türck's solution, and this enabled both megakaryocyte counts and total nucleated-cell counts to be made. The mean megakaryocyte concentration in the marrow of 23 healthy young adults was $4{\cdot}0 \pm 1{\cdot}1$ per 10,000 nucleated cells. The megakaryocyte concentration seemed to parallel the granulocyte count more closely than the erythrocyte or lymphocyte count. Examinations of the marrow aspirated at different times from the same subjects revealed a variation of less than 30% in 8 of 9 cases. *P. C. Reynell*

153. **The Cytological Diagnosis of Carcinoma by the Examination of Bronchial Secretions.** (Zytologische Krebsdiagnostik aus dem Bronchialsekret)
W. Strupler. *Practica Oto-Rhino-Laryngologica* [*Pract. oto-rhino-laryng., Basel*] **12**, 257–265, 1950. 18 figs.

The examination of smears from secretions as a help in diagnosis has been practised for some years, notably in carcinoma of the cervix. The same technique has been successfully used in the examination of bronchial secretions. In 6 cases the tumour was seen through the bronchoscope, but the biopsy forceps could not reach it; in each of these cases the smear showed malignant cells. In 4 cases a tumour was suspected, but was not visible through the bronchoscope; in these also the smear was positive for malignant cells, and the diagnosis of cancer was confirmed at subsequent operation or necropsy.

William McKenzie

154. **Disturbance of Liver Function in Rheumatism.** (О нарушении функционального состояния печени при ревматизме)
M. L. Lorman. Клиническая Медицина [*Klin. Med., Mosk.*] No. 1, 86–87, 1951.

Severe disturbance of liver function is rarely found in patients suffering from rheumatism, but milder changes are not uncommon. The author describes 76 cases of rheumatoid arthritis which were investigated from this point of view. In 15 cases, in 7 of which there was no heart lesion, the liver showed marked enlargement, but in all it returned to normal on recovery. In 66 cases there was disturbance of water metabolism, the 24-hourly output being only 65 to 75% of the intake, and recovery was followed by diuresis. In 59 cases McClure's blister test was positive. The surface tension of the urine was lowered in 66 cases, due in all probability to the presence of bile acids. Ehrlich's aldehyde reaction for urobilinogen was positive in 54 cases, and the Takata-Ara reaction in 13. These returned to normal after recovery. *L. Firman-Edwards*

Microbiology

155. **Some Biological Implications of Studies on Influenza Viruses. I. The Process of Infection by the Virus. II. Reproduction and Variation in Influenza Viruses. III. The Ecological Approach to the Common Virus Disease of Today**
F. M. BURNET. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **88**, 119–180, Feb., 1951. 2 figs., bibliography.

156. **The Multiplication of Influenza Viruses in the Fertile Egg. A Report to the Medical Research Council**
L. HOYLE. *Journal of Hygiene* [*J. Hyg., Camb.*] **48**, 277–297, Sept., 1950. 9 figs., 31 refs.

[This important paper, from the Public Health Laboratory, Northampton, is too long for its details to be adequately abstracted, but the following summarizes the conclusions reached by the author.]

On the basis of studies of the growth of influenza-A virus in the developing egg its life cycle is probably as follows. "The infective elementary body [evidently] consists of an aggregate of soluble antigen and specific antigens enclosed in a lipoidal envelope. The specific antigens are probably identical with the agglutinin and are capable of uniting with receptor substances of a mucoprotein nature in the wall of the host cell. The complex is also capable of destroying the mucoprotein of the cell wall so that the virus is able to penetrate to the interior."

On penetration, the virus disintegrates into its component units of macromolecules of soluble antigen, which are probably nucleoprotein in nature and, although particulate, are considerably smaller than the elementary body. They then begin to multiply and a fifty-fold increase in amount occurs between the second and fourth hours. During this phase there is no comparable increase of either agglutinin or specific antigen and these factors do not appear in quantity until after the fourth hour. Even so, the main increase in agglutinin and specific antigen occurs at a later stage, when the virus is about to be released from the cell. But it is probable that the increase in specific antigen is due to the laying down of more molecules at the edges of the original molecules, which therefore act as pattern molecules, in this way ensuring serological identity of the strain on passage. During these stages the virus is almost non-infective, and it is not until the virus is liberated from the cell wall that infectivity is regained.

The final stage in the development of the virus would appear to depend on the nature and vigour of the attack of the developing virus on the cell wall. In consequence of this there is a tendency for protrusion of cytoplasm to occur, probably due to weakening of the cell walls. These protrusions contain aggregating virus, and when they become detached they shrink, partly as a result of increasing permeability of the membrane and partly as a result of the increasing aggregation of the virus protein. This leads to the formation of the spherical elementary bodies and filaments of various types which are the infective particles known to us from electron micrography.

R. Hare

157. **A New Technique for the Determination of Fungistatic Activity against Dermatophytes.** (Nouvelle technique de détermination du pouvoir fungistatique à l'égard des dermatophytes)
R. VANBREUSEGHEM. *Archives Belges de Dermatologie et de Syphiligraphie* [*Arch. belges Derm. Syph.*] **6**, 238–241, Dec., 1950. 2 refs.

The author's method consists in cultivating the fungi on hairs *in vitro*. A small fragment of the fungus culture is placed upon the hair, where it develops in a manner identical with that seen in its saprophytic life. The following fungi were used in the experiment; *Nocardia asteroïdes*, *Pityrosporum ovale*, *Epidermophyton floccosum*, *Microsporum duboisi*, and *M. canis*. The test substance was propylene phenoxetol and it was found that fungus growth was entirely inhibited in an atmosphere of this substance, but that dipping the hair in the pure substance or in a 1% solution before inoculation only delayed growth.

James Marshall

BACTERIA

158. **A Comparative Study of Methods of Isolating *Mycobacterium tuberculosis***
D. GIFFORD, F. MCKINLEY, and C. A. HUNTER. *American Journal of Public Health* [*Amer. J. publ. Hlth*] **41**, 164–167, Feb., 1951. 8 refs.

A review is given of various digestive agents used in the preparation of sputum for the culture of *Mycobacterium tuberculosis*. A comparison was made of the efficiency of sodium hydroxide and trisodium phosphate as digestive agents and also of the efficiency of Löwenstein's and Petragnani's culture media.

The sputum used was mostly from food handlers, sent for routine check, or from patients with suspicious clinical symptoms or suggestive *x*-ray findings; the number of negative cultures was therefore high. About 2 ml. of sputum was added to an equal amount of 10% trisodium phosphate or 4% sodium hydroxide containing phenol red as an indicator. The mixture was shaken for 10 minutes and then centrifuged for 15 minutes at 3,000 r.p.m. The specimens digested with sodium hydroxide were then neutralized with 2N hydrochloric acid. The deposit was inoculated on to slopes of Löwenstein's and Petragnani's media and incubated for 8 weeks at 37° C.

In a series of 3,788 specimens only 2,368 were of sufficient volume for both methods of digestion; of these last, 574 (24·23%) were positive; 447 (18·87%) were positive with both digestion methods, 74 (3·12%) were

positive with trisodium phosphate only, and 53 (2·23%) positive with sodium hydroxide only. In the same series the contamination rate with sodium hydroxide was 1·03%, whereas the rate with trisodium phosphate was 3·85%. A slightly greater number of positive cultures was obtained with Löwenstein's medium than with Petragnani's, regardless of the method of digestion.

A. G. S. Heathcote

159. **Studies on the Virulence of Tubercle Bacilli. The Relationship of the Physiological State of the Organisms to their Pathogenicity**

H. BLOCH. *Journal of Experimental Medicine* [*J. exp. Med.*] **92**, 507–526, Dec., 1950. 7 figs., 35 refs.

Previous investigations had suggested that a petroleum ether-soluble material ("cord factor") extracted from virulent tubercle bacilli was associated with virulence. A greater amount of cord factor could be extracted from young than from older cultures, and therefore a comparison of the virulence of young and old cultures was carried out.

When 3-day cultures in a fluid medium of bovine or human strains were inoculated intravenously into mice, animals began to die in less than one week and only about 50% survived after 2 weeks. The death rate followed a logarithmic curve. In the first mice to die macroscopic lesions were seen only on the heart, as pin-point yellow spots; histologically, they appeared as acute inflammatory foci containing vast numbers of bacilli. In mice which survived longer similar lesions were found in the lungs and other tissues. The inoculation of 3-week-old cultures, diluted to the same density as the young cultures, produced classical tuberculosis in the mouse; the heart showed no lesions. Signs of the disease did not appear until after 2 weeks and the death rate did not follow a simple logarithmic curve. Experiments suggested that there were no more bacilli in 3-day cultures than in 3-week cultures standardized to the same density. Similar results were obtained with other strains of mice. A 1-day culture proved less virulent than a 3-day culture; there was some indirect evidence that the very young organisms had formed less cord factor. A similar acute septicaemic form of tuberculosis was produced in rabbits with 3-day cultures. The acute form of tuberculosis produced in mice and rabbits probably corresponded to the Yersin type. It is suggested that this form of disease is possibly not uncommon as a natural infection of man. *D. G. ff. Edward*

160. **A Study of Streptomycin Resistance in *Micrococcus pyogenes* var. *aureus***

A. R. ENGLISH and A. MCCOY. *Journal of Bacteriology* [*J. Bact.*] **61**, 51–56, Jan., 1951. 1 fig., 6 refs.

With a streptomycin-sensitive strain of *Staphylococcus pyogenes* var. *aureus* derived from a single cell, resistance was produced in one stage in the Agricultural Bacteriology Department, University of Wisconsin, by inoculating liquid medium containing 200 units streptomycin per ml. Growth occurred in 1 of 100 inoculations, at 100 times the minimum inhibitory concentration for the parent culture. Normal growth curves developed with 0·01 unit per ml. whereas in 0·1 unit per ml. the lag phase was longer and the final density of organisms lower. Serial transfers at the lower level produced no increased resistance, but in higher concentration a 5-fold increase developed.

Streptomycin-resistant organisms grew better on a semi-synthetic medium than their streptomycin-sensitive parent, and this characteristic enabled a resistant culture to be selected by serial transfer from the sensitive parent strain in the absence of streptomycin.

The authors believe that their experiments support the hypothesis that streptomycin resistance arises by selection of resistant mutant cells, and not by adaptation. *Peter Story*

161. **Subacute Bacterial Endocarditis Caused by Coagulase-negative *Staphylococcus albus***

H. MATHEW. *Lancet* [*Lancet*] **1**, 146–148, Jan. 20, 1951. 17 refs.

Two consecutive cases of subacute bacterial endocarditis are described in which a coagulase-negative strain of *Staphylococcus pyogenes* var. *albus* was the causative organism. They presented typical signs and symptoms of subacute endocarditis and were remarkably alike clinically. The method used for testing for coagulase was that of Fisk (*Brit. J. exp. Path.*, 1940, **21**, 211). During the 2 weeks following the hospitalization of the first patient 7 blood cultures were carried out and all grew a coagulase-negative *Staph. pyogenes*. No other organisms were grown, and the blood was withdrawn by 4 different operators using different skin-cleansing agents. Pus from an acne pustule and blood obtained from the sternal marrow grew a coagulase-negative staphylococcus. The organism was penicillin-sensitive, with a coefficient of resistance of 1. The patient's serum had a higher antibody titre for this particular organism than had pooled serum. The patient was treated with penicillin, 250,000 units 3-hourly, but died on the 19th day of penicillin therapy. Necropsy was performed 4 hours after death and the heart was opened aseptically. The blood was sterile, but the aortic valve yielded a coagulase-negative staphylococcus similar to, if not identical with, the organism previously isolated.

Blood culture from the second patient produced coagulase-negative staphylococci of the same species on five occasions in 5 days. No other organism was isolated. The coefficient of resistance to penicillin was 1. The patient was treated with 250,000 units of penicillin 3-hourly, but died on the 34th day of treatment. The heart was opened aseptically and from the heart blood and aortic valve was grown a coagulase-negative strain of staphylococcus corresponding to the one isolated during life on blood culture.

Pericarditis and pericardial effusion produced by focal embolic infarction of the myocardium were found in both cases, although these are rarely present in cases of subacute bacterial endocarditis. The presence of Aschoff bodies of recent formation supports the view that subacute bacterial endocarditis is often superimposed on a valve in the presence of active rheumatic carditis. *R. Hodgkinson*

IMMUNITY

162. **Syringe Needles and Mass Inoculation Technique**
A. FLEMING and A. C. OGILVIE. *British Medical Journal* [*Brit. med. J.*] **1**, 543–546, March 17, 1951. 3 refs.

War Memorandum No. 15, issued by the Medical Research Council, advocated that in mass inoculations one syringe should be used, with a fresh sterile needle for each patient. Risks inherent in this practice have now been pointed out, as bacteria and tissue fluids may be sucked into the syringe from the needle as it is removed. It is now shown that the needle can be effectively sterilized while still attached to the syringe by immersing it for half its length in hot liquid paraffin. Fluid ejected through a needle, previously heavily contaminated with a bacterial culture and afterwards immersed for at least 4 seconds in oil at a temperature above 120° C., was sterile. For routine use 10 seconds' immersion in oil at 130° to 150° C. is recommended. When oil is not available, 10 seconds' immersion in boiling water is effective.

When a syringe and needle were used for subcutaneous inoculations, in 6 out of 50 observations tissue fluids were demonstrated in the needle and were present in the fluid ejected through the needle subsequently. When the needle was immersed in oil after inoculation, tissue fluids were not demonstrated in the fluid subsequently ejected through the needle.

When inoculations were made against pressure, reflux into the syringe sometimes occurred. Its occurrence depended on the pressure and on the angle at which the needle was inserted. There were also differences according to the position of the plunger and between individual syringes. If in making an injection even against pressure the syringe was completely emptied and pressure was kept on the plunger while withdrawing the needle, no reflux into the syringe occurred. It is therefore recommended that for mass inoculation only one dose should be taken into the syringe. After injecting this, pressure should be maintained on the plunger while withdrawing the needle and the needle should then be sterilized, without removal, by immersion for 10 seconds in oil at over 130° C. *D. G. ff. Edward*

163. **A Hemolytic Modification of the Hemagglutination Test for Antibodies against Tubercle Bacillus Antigens**
G. MIDDLEBROOK. *Journal of Clinical Investigation* [*J. clin. Invest.*] **29**, 1480–1485, Nov., 1950. 12 refs.

Sheep erythrocytes sensitized with extracts of tubercle bacilli, or with products of culture filtrates, are agglutinated by the sera of tuberculous individuals. This haemagglutination is the basis of the Middlebrook–Dubos reaction. In a modification here described complement, previously absorbed with sheep erythrocytes, is added when the reaction is complete. Haemolysis was often observed instead of haemagglutination where the sera were from tuberculous individuals or from immunized animals, but not where the sera were from non-tuberculous cases. Haemolytic titre was not obviously related to haemagglutination titre in the small number of sera examined. The two tests possibly measure different antibodies. *J. E. M. Whitehead*

164. **Maternal and Foetal Titres of Antistreptolysin and Antistaphylolysin at Different Stages of Gestation**
B. VAHLQUIST, R. LAGERCRANTZ, and F. NORDBRING. *Lancet* [*Lancet*] **2**, 851–853, Dec. 23, 1950. 43 refs.

Serum samples from 53 foetuses obtained by legal abortion after periods of gestation varying from 16 weeks to full term were examined for antistreptolysin and antistaphylolysin, and the values obtained compared with those for the sera of the mothers, taken at the same time. Up to the 22nd week of gestation the titres of antistreptolysin and antistaphylolysin in foetal sera were markedly less than the titres in the corresponding maternal sera; after this the foetal serum titres steadily approached the maternal serum titres and occasionally exceeded them. The authors ascribe this change to the steady increase in intimacy between the foetal and maternal circulations as gestation advances. Premature infants born between the 30th and 39th week of gestation showed a close correspondence between foetal and maternal titres for antistreptolysin, but not quite so close for antistaphylolysin.

[As substances other than specific antibody can inhibit the activity of streptolysin, antistreptolysin titres are always open to suspicion. To say that in Barr, Glenny, and Randall's work the titres of diphtheria antitoxin in mother and foetus were " about equal " is surely to miss the most interesting point—that the titre of cord-blood samples was often markedly above that of maternal samples.] *C. L. Oakley*

165. **Use of the Pertussis Agglutinogen Skin Test in a Well Baby Clinic**
N. BARYSH. *Pediatrics* [*Pediatrics*] **7**, 48–51, Jan., 1951. 14 refs.

This paper records an investigation of the use of pertussis agglutinogen as a skin test to determine susceptibility or immunity to pertussis in 234 normal infants from one week to 9 months old. Acid-precipitated agglutinogen consisting of 100 units of the lyophilized material was added to 1 ml. of normal saline solution, and 0·1 ml. of the dissolved material was injected intracutaneously into the forearm of the infant. The area of induration was measured at the end of 24 hours: an area of redness and/or induration of 10 mm. or more was considered an immune or positive reaction; an area of redness alone or of induration of less than 10 mm. was considered to be a semi-positive immune reaction; no skin response was a negative reaction. Of 100 infants who had been immunized before the skin test, 92% gave immune reactions. Of 134 infants skin tested before pertussis vaccine immunization, 83% gave negative skin reactions; 111 of these 134 were re-tested after immunization and 92% gave a positive response.

It is concluded that the pertussis skin agglutinogen test can be used to ascertain the efficacy of materials employed in pertussis prophylaxis; that it is a reliable indicator of the immune response of an infant to pertussis immunization; and that it provides an effective method of determining the infant who is still susceptible to infection after pertussis vaccination.

B. S. P. Gurney

Paediatrics

166. ***Salmonella typhi-murium* Infections in Infancy.** (L'infection à *Salmonella typhi-murium* du nourrisson)
J. MARIE, P. SERINGE, L. LE MINOR, and E. ELIACHAR.
Semaine des Hôpitaux de Paris [*Sem. Hôp. Paris*] **27**, 615–621, Feb. 26, 1951. 2 refs.

The importance of *Salmonella typhi-murium*, or Aertryck's bacillus, as a cause of neonatal disease is perhaps not generally realized. The diversity of the clinical pictures of this infection and the difficulties of infant stool culture contribute to this neglect. In this paper the authors outline the main clinical types of the infection: septicaemia, gastro-enteritis, and localized parenteral infections.

Two small epidemics (12 and 8 cases respectively) of *Salm. typhi-murium* septicaemia are reported. Although the blood culture was positive in all cases, the stools were positive in only 3 and serological evidence of infection present in only 6. In the first epidemic 6 died, and in the second 3. No chloramphenicol was used in the first, but it was used in 7 cases in the second outbreak, the untreated patient being among those dying. The symptomatology was varied. A hectic, " gothic profile " type of fever was usual, but afebrile cases were noted and in them the prognosis was particularly grave. Gastro-intestinal symptoms were not constant. Meningitis, otitis media, and pulmonary, hepatic, and renal involvement were all encountered, but only meningitis appeared to affect the outcome. The course of the disease was prolonged whatever the result and in one case death occurred 5 months after the onset. Details of treatment are not given.

Salm. typhi-murium gastro-enteritis has been described particularly from South America. The authors briefly summarize the literature. The picture is that of any gastro-enteritis and it is distinguishable only by bacteriological methods. All degrees of severity are encountered, but in epidemics the mortality rate ranges between 10% and 30%. Convalescent and healthy carriers are not uncommon.

Lastly brief mention is made of localized parenteral infections with the organism without either septicaemia or gastroenteritis. It is suggested that the nasopharynx is a possible portal of entry in these cases.

T. A. A. Hunter

167. **Epidemiology of *Salmonella typhi-murium* Infections.** (Epidémiologie de l'infection à *Salmonella typhi-murium*)
P. SERINGE, J. MARIE, E. ELIACHAR, and L. LE MINOR.
Semaine des Hôpitaux de Paris [*Sem. Hôp. Paris*] **27**, 621–623, Feb. 26, 1951. 1 ref.

On the basis of the literature the authors summarize the epidemiology of *Salmonella typhi-murium* infections. Possible reservoirs of infection are numerous. Many mammals, birds, and insects are susceptible to the organism, which may be present in both milk and eggs. Healthy human beings may be carriers of the bacillus, whether or not they have had a clinical infection. Carrier rates as high as 2% in a healthy population have been reported. The organism is a potential contaminant of drinking water. In view of this widespread distribution of the infecting agent only the highest possible standard of hygiene in the care of infants can prevent outbreaks among them. Evidence is quoted to show that anything less than this highest standard can and does introduce the infection. *T. A. A. Hunter*

168. **Bacteriology and Immunology of *Salmonella typhi-murium* Infections.** (Bactériologie et immunologie de l'infection à *Salmonella typhi-murium*)
L. LE MINOR, J. MARIE, P. SERINGE, and E. ELIACHAR.
Semaine des Hôpitaux de Paris [*Sem. Hôp. Paris*] **27**, 623–625, Feb. 26, 1951.

This is an account of the bacteriological techniques used in the investigation of *Salmonella typhi-murium* infections by stool and blood culture. Cultural procedures and strain differentiation by biochemical and serological methods are described in detail. The procedure for serum agglutinations is also briefly mentioned.

[The paper should be read in the original by specialists in this field.] *T. A. A. Hunter*

169. **The Treatment of *Salmonella typhi-murium* Infections.** (Le traitement de l'infection à *Salmonella typhi-murium*)
J. MARIE, P. SERINGE, L. LE MINOR, and E. ELIACHAR.
Semaine des Hôpitaux de Paris [*Sem. Hôp. Paris*] **27**, 625–630, Feb. 26, 1951. Bibliography.

Infants suffering from infections due to *Salmonella typhi-murium* should be nursed with a strict barrier technique. In particular it is urged that the staff who prepare feeds should have no direct contact with such cases. Domiciliary treatment of suitable cases is advocated and a plea is made for the routine instruction of mothers in nursery and kitchen hygiene.

Standard supportive treatment is required in this disease, but it is not discussed in detail. Penicillin and the sulphonamides have been shown to be ineffective. Streptomycin has a definite bacteriostatic effect on the organism, but it seems incapable of eradicating the infection, and relapse follows its withdrawal. It retains a place in the chemotherapy of the disease because it can be given parenterally and, particularly, intrathecally. Chloramphenicol is the antibiotic of choice. Laboratory and clinical studies have shown its effectiveness, but it must be given over a considerable period. The authors recommend a total of 0·5 to 1 g. daily by mouth in 2 or 4 doses. Within these limits the dose is 150 mg. per kg. of body weight. This dosage should be maintained for not less than 3 weeks. Contrary to expectation no difficulty was found in getting infants to swallow the capsules, but vomiting at times caused trouble. A

comparison of the results in two small epidemics suggested that the use of chloramphenicol reduced the mortality of the septicaemic form of the infection by nearly 50%. *T. A. A. Hunter*

170. **Thirty-six Years' Experience of the Treatment of Pylorospasm in Newborn and Young Infants with Papaverine.** (36 Jahre meiner Papaverintherapie der Spasmen des Pylorus bei Neugeborenen und jungen Säuglingen) E. MAYERHOFER. *Annales Paediatrici* [*Ann. paediatr., Basel*] **176**, 73–81, Feb., 1951. 13 refs.

The author lays stress on having introduced, in 1913, the treatment of pylorospasm with papaverine. Since that time he has treated hundreds of infants with this drug, provided that an early diagnosis had been made. In the presence of a palpable pyloric tumour papaverine has little or no effect, still less in hypertrophic stenosis of the pylorus. The author is of the opinion that the functional spasm resembles the allergic spastic vomiting, both of which may lead to a muscular hypertrophy. To avoid such a development he recommends the combination of papaverine 0·01 g. with amidopyrine 0·05 g. 3 to 4 times daily. In cases of vomiting, suppositories, medicated enemata, or injections of papaverine hydrochloride are indicated. *Franz Heimann*

171. **Hirschsprung's Disease**
M. BODIAN, C. O. CARTER, and B. C. H. WARD. *Lancet* [*Lancet*] **1**, 302–309, Feb. 10, 1951. 10 figs., 20 refs.

The material for this important study of Hirschsprung's disease consists of 40 consecutive cases treated at the Hospital for Sick Children, Great Ormond Street, London. All cases were confirmed by histological examination of the affected bowel. The authors define the disease by pathological and clinical criteria, give a genetic study of 37 of the families, record the results of the new operative treatment by rectosigmoidectomy in 37 cases, and discuss the pathology and pathogenesis.

True Hirschsprung's disease is a congenital malformation, with incoordination of peristalsis in a variable length of terminal bowel, due to absence of the intramural ganglion cells in the affected part and a dysplasia of the associated autonomic nerve-plexuses. This agenesis of nerve-cells results in narrowing of the length of gut affected and produces dilatation of the bowel above. Although this can be confirmed only by microscopical examination of the bowel, the diagnosis can be made radiologically, a barium enema clearly showing the terminal narrow length of large bowel with the dilated bowel above. This radiological picture distinguishes Hirschsprung's disease from the much commoner condition of idiopathic megacolon, where dilatation extends right down to the anus.

The genetic study differs from other published reports in the much larger number of cases, and in the accurate radiological and histological diagnoses. To 37 cases the examination of all the siblings of the families added 4 more cases, all in boys; this gave a total of 41 cases, of which 38 were in boys and 3 in girls. It was judged from inquiries, without examination, that there were no cases of the disease among the parents, grandparents, uncles, aunts, and first cousins of the patients. The authors discuss in detail their findings in regard to family incidence and conclude that there is a genetic determination of the disease, with a 1 in 5 chance of affection in a male sibling and a much smaller chance in a female sibling. Similar family investigations by other workers are needed, including an examination of the children of patients successfully treated, before the nature of the genetic factors can be determined.

Treatment by the operation of rectosigmoidectomy [introduced at the Boston Children's Hospital by Swenson and Bill about 3 years ago] was carried out in 37 cases. There were 3 deaths, 2 under anaesthesia and one from peritonitis. Of 32 children who have been followed up over periods of 6 months to 2 years, all are in excellent general condition, passing regular motions (about half assisted by laxatives), and all but one have attained an average weight. In 3 cases there has been anal stricture, which has not retarded general progress.

As to the morbid anatomy, all but one of these cases were of the " short and intermediate segment " variety, involving the rectum and sigmoid only; and in an aggregate of 90 histologically verified cases (including the authors' cases), 82 were of this short and intermediate variety, while 8 cases were of the " long segment " variety, where the abnormal bowel extended to the splenic or hepatic flexure and in one case for a short distance up the terminal ileum. In this much less common variety the prognosis is bad, and most of the deaths occur in this group. The morbid histology of all the cases of the present series showed a complete absence of intramural ganglion cells in the affected segment, with an increase in size of the intramural autonomic nerve fibres.

The authors cautiously discuss the pathogenesis. Their view, " purely theoretical " and based on the morbid anatomy and histology, is that there is a disturbed development of the intramural ganglion cells, which is genetically determined; and that the time of occurrence of this error of development determines whether the long, intermediate, or short variety develops.

Finally, the paper contains a brief report and discussion of a unique case where the aganglionic bowel extended from the anus to the duodeno-jejunal flexure and where there were no intramural nerve fibres throughout this whole length of large and small bowel. This case, it is suggested, may be " a particularly severe variant of Hirschsprung's disease ". *Charles McNeil*

172. **Acute Obstructive Laryngotracheitis and Laryngotracheobronchitis. Report of an Outbreak**
J. O. FORFAR, K. R. KEAY, and J. THOMSON. *Lancet* [*Lancet*] **1**, 181–186, Jan. 27, 1951. 33 refs.

An outbreak of acute obstructive laryngotracheitis and laryngotracheobronchitis is described, apparently the first of its kind in Britain: 22 cases were treated in a population of 182,000. The age incidence was from 4 months to 9 years. Acute laryngeal obstruction was present in all cases, but it should be noted that acute non-obstructive laryngitis and laryngotracheitis were prevalent in the population at the time. In all cases respiratory obstruction was of sudden onset, simulating

on occasion an inhaled foreign body. On admission, the main features were the respiratory distress and prostration. Cyanosis was not striking, but in the more severe cases ashen pallor was found to be a sign of ill omen. Laryngoscopy was at first performed to rule out the presence of membrane, but since it worsened the condition it was abandoned after the first 3 cases, though the authors recommend its use in sporadic or doubtful cases. Chest examination was not particularly helpful, and radiography revealed normal lung fields or sometimes terminal bronchopneumonia. The leucocyte count varied from 5,000 to 33,000 per c.mm. and was of no help. Swabs taken from the pharynx and also from the respiratory tract post mortem did not reveal any predominating organism, except in one case where *Corynebacterium diphtheriae* was isolated; investigations into the immunological history of this patient and the lack of response to diphtheria antitoxin gave the authors ground to think this child was a carrier. The course of the disease was short: 4 patients died, having been ill for from 10 hours to 3 days; 18 recovered, convalescence being established in a week.

Treatment was with steam, antibiotics, adequate fluids, and avoidance of atropine and respiratory depressants. Tracheotomy and laryngoscopy are freely recommended by many writers, though the authors were not convinced that either was of great value. Some of the patients treated conservatively seemed to be as ill as those who died after laryngoscopy. Of the antibiotics, penicillin was used in all cases (with sulphamezathine) and aureomycin in the severe cases. Oxygen could be given only for limited periods because of the distress of the patient on being in any way confined.

The necropsy findings were those usually reported in this condition. In one case there was almost complete occlusion of the larynx: tracheotomy had been performed in this case. Others showed varying degrees of patency of the larynx. There were toxic changes in the liver and myocardium. The authors feel that toxic effects are as important as the laryngeal obstruction in this condition. Though antibiotics are not necessarily specific, they must be employed if only to combat secondary invasion. The aetiology of the condition still remains unknown. *J. G. Jamieson*

173. **Congenital Verbal – Auditory Agnosia. (Word Deafness)**
I. W. KARLIN. *Pediatrics* [*Pediatrics*] 7, 60–68, Jan., 1951. 3 figs., 13 refs.

The author first describes the accepted features of congenital word deafness, and then reports the case of a Jewish boy, aged 6, whose general development was only a little behind the average but whose speech was very limited. No gross physical defects were noted. Intelligence tests revealed relatively slight deficiency, and although the parents were convinced that the child had heard sounds, he appeared unable to comprehend speech. At the first audiometric test it was decided that the child had a profound nerve deafness—98·4% on each side; there was a total absence of nystagmus with the cold caloric test. However, since the child was able to decide correctly which of 3 toys—a snapper, a rattle, and a horn—had been sounded behind him at a distance of 15 feet (4·5 m.) and could say some things, it was considered that further investigation was necessary. Psychogalvanic skin-resistance audiometric tests showed that the child's auditory impairment was less than that indicated by the ordinary hearing tests. The findings tended to confirm the diagnosis of congenital word deafness. The report on the electroencephalogram was: "greater than usual per-cent-time of potentials slower than 8 seconds, and greater than usual bilateral asynchrony and base-line irregularity. Impression: activity slightly slower than normally expected for the age". A new term, "congenital verbal auditory agnosia", is suggested for word deafness.

[This is not a very satisfying contribution to this interesting problem. The author does not seem to have proved even his diagnosis, since he neglects completely the fact that the auditory pathway was most probably affected at a much lower level than the cortex, if we are to believe the results of the caloric test. On this doubtful case he has built up a not very original structure of discussion.] *Fergus R. Ferguson*

174. **Some Typical Data from Cases of Pink Disease**
C. S. HICKS. *British Medical Journal* [*Brit. med. J.*] 1, 317–322, Feb. 17, 1951. Bibliography.

In 16 cases of pink disease Cheek and Stace found a low plasma sodium level to be the only significant biochemical finding. This they assumed to be due to adrenal cortical hypofunction. Treatment with salt produced uniformly good and rapid results: 8 g. daily was the dose for mild cases and this was supplemented by 3 mg. of deoxycortone acetate intramuscularly on alternate days in severe cases.

Jaudon's work on cortical insufficiency in infancy is referred to, and by analogy the author suggests that subacute or chronic cortical hypofunction may be present after pink disease and that this hypofunction may also be responsible for the "cryptic" manifestations of pink disease: psychological instability, failure to thrive, lassitude, recurrent catarrh, and allergic manifestations, all of which, it is concluded, may be relieved by common salt, with the addition of corticosteroid in severe cases. The incidence of pink disease in Australia is attributed to the lack of salt in weaning diets generally in use: this may be the "exacerbating factor". The possibility that mercury idiosyncrasy may be of aetiological significance is given brief mention and it is suggested that mercury may depress adrenal cortical function.

[In view of the fact that a history of mercury ingestion is obtained in nearly every case of pink disease and that excretion of excessive quantities of mercury in the urine is also to be observed in the majority, many authorities feel that mercury is the essential factor in the disease. The falling hair, stomatitis, loss of teeth, and the rash are typical of mercury poisoning, and the loss of plasma sodium may well be the result of the excessive sweating. The geographical variations in incidence may prove to be associated with the local sale of teething powders or the use by practitioners of mercury and chalk.]
Wilfrid Gaisford

Medicine : General

175. **Bronchial Asthma Treated by Bilateral Resection of the Vagus. A Report of Six Cases**
C. A. CLARKE. *Lancet* [*Lancet*] **1**, 438–440, Feb. 24, 1951. 7 refs.

Six asthmatic patients in whom there was no obvious cause for the attacks and in whom medical treatment had failed were chosen for operation. All branches of the vagus nerve going to the posterior pulmonary plexus, as well as the main branch to the anterior plexus, were divided: 3 weeks separated the operations on the two sides. The result of the operation was disappointing. Two patients had an excellent result, one improved only to relapse, and the remainder showed slight improvement only. *A. W. Frankland*

METABOLIC DISORDERS

176. **Persistent Hypokalaemia Requiring Constant Potassium Therapy**
K. KJERULF-JENSEN, N. B. KRARUP, and A. WARMING-LARSEN. *Lancet* [*Lancet*] **1**, 372–375, Feb. 17, 1951. 5 figs., 4 refs.

A married woman, now aged 35, had a lymphocytic meningitis when 28 years old, followed by periodic generalized oedema without albuminuria, the oedema starting about 14 days before menstruation and disappearing when menstruation began. No abnormalities were detected. She had had 2 normal pregnancies before the meningitis and one normal pregnancy 2 years after; this was followed by amenorrhoea, the intermittent oedema continuing. When aged 33 she again became pregnant and the oedema disappeared. During the fifth month she had severe peritonsillitis and aborted a month later. She then developed hypotension, bradycardia, muscular weakness, paraesthesiae, and loss of weight. Addison's disease was diagnosed and 10 mg. deoxycortone was given daily for 10 days, when she had several heart attacks and collapsed. The serum potassium level was 1·38 mEq. per litre and the electrocardiogram was typical of hypokalaemia.

During the next 6 months the patient remained in bed, with some improvement. Anorexia, muscular weakness, amenorrhoea, and the intermittent oedema remained. Serum potassium level was 2·5 mEq. per litre. Oral administration of potassium salts was then started with a single dose of mixed phosphates equivalent to 15 g. of potassium. Serum potassium level was 4·9 mEq. per litre after 3 hours and the patient collapsed. After a few days, 3 g. potassium daily were given, the serum content reaching 5·13 mEq. per litre after 10 days' treatment. The daily dose was then reduced to 1·5 g. potassium, with 0·8 g. sodium (as sodium chloride). After a further month the patient felt well and was discharged. Menstruation had restarted. The patient's health has been maintained on this dose. On several occasions she has reduced or omitted her daily dose for several weeks. This has always resulted in a deterioration and a fall in serum potassium level to about 2·7 mEq. per litre. Adequate oral potassium restores her to normal in a few days. The intermittent oedema is still present and has not been affected by the potassium therapy. When the patient took 3 g. potassium daily her average daily urinary excretion was 5·65 g. of potassium.

The cause of the continuing deficiency of potassium is unknown. The authors suggest a disturbance of some central regulating mechanism. *M. Lubran*

177. **Treatment of Chronic Renal Potassium Deficiency**
H. G. DAVIDSEN, K. KJERULF-JENSEN, and N. B. KRARUP. *Lancet* [*Lancet*] **1**, 375–378, Feb. 17, 1951. 8 figs., 7 refs.

A woman aged 44 with bilateral hydronephrosis and a non-functioning left kidney developed marked hypokalaemia 4 months after implantation of her right ureter into the pelvic colon to relieve a vesico-vaginal fistula. Serum potassium level was 1·12 mEq. per litre, that of plasma bicarbonate low, and of other blood electrolytes normal. Intravenous administration of an isotonic solution containing, per litre, 36 mEq. of postassium (as neutral phosphates) and 120 mEq. of sodium (as bicarbonate) raised the bicarbonate level, but did not alter that of potassium. Serum level of phosphate rose, and of calcium fell to 1·8 mEq. per litre, tetany resulting. There was no diuresis, and generalized oedema occurred. The patient became moribund and was given orally 10 ml. of 10% potassium chloride solution every 15 minutes for 14 doses. A profuse diuresis started after one hour and the oedema disappeared, but tetany occurred a few hours later. This responded to calcium gluconate, and normal serum levels of potassium, calcium, and phosphate were obtained with oral potassium chloride and calcium lactate during the next fortnight.

The patient discharged herself, but relapsed after 17 days. Following the administration of 10% potassium chloride and sodium bicarbonate powder, there was fluid retention, serum phosphate level fell, but that of calcium was unaltered. Serum potassium level rose slowly until the 4th day, when it quickly rose to 8 mEq. per litre, the phosphate level rising too. By then, 1,072 mEq. of potassium had been given, yet the potassium content of the erythrocytes remained low. Unfortunately at this stage the patient developed tuberculous pneumonia and died. A piece of iliopsoas muscle showed 60% of the normal potassium content and three times the normal sodium content.

In rabbits administration of sodium phosphate orally or intravenously caused the serum level of phosphate to rise and of calcium to fall, but had no effect on that of

potassium. Intravenous infusion of potassium chloride had no effect on serum phosphate level.

The authors suggest that chronic hypokalaemia should be treated with oral hypertonic potassium salts containing 3 equivalents of potassium to 1 of phosphate and 2 of chloride or bicarbonate. *M. Lubran*

178. **Skeletal and Periarticular Manifestations of Hypervitaminosis D**
W. R. CHRISTENSEN, C. LIEBMAN, and M. C. SOSMAN. *American Journal of Roentgenology and Radium Therapy* [*Amer. J. Roentgenol.*] **65**, 27–41, Jan., 1951. 4 figs., bibliography.

Five cases in which unusual skeletal and periarticular changes were considered to be due to hypervitaminosis D are described. All the patients had a history of arthritis and had been taking daily doses of over 50,000 units of vitamin D for more than a year. Radiographs showed a combination of generalized osteoporosis and soft-tissue calcifications, occurring mainly in the periarticular structures such as synovial cavities, bursae, tendon sheaths, etc., in the form of amorphous or smoothly lobulated masses. The changes appeared to be reversible for a time and in most cases improved markedly when vitamin D was withdrawn, as did the raised serum calcium level and impaired renal function which was found initially in every case.

The differential diagnosis and aetiology of the condition are discussed. It must be distinguished from calcinosis and from changes which may occur in hyperparathyroidism and chronic nephritis. The suggestion is made that vitamin D_2 (activated ergosterol) is almost invariably responsible for the metastatic calcifications in cases of hypervitaminosis. Animal experiments indicate that vitamin D_3 is a more effective antirachitic, and far less toxic, than vitamin D_2.

[All these cases are unusual in that there was a history of pre-existing arthritis. Although this may not have been directly responsible for any of the changes described, it seems probable that its presence would modify the manifestations of hypervitaminosis D.]
J. A. Shiers

179. **Some Recent Studies of Porphyrin Metabolism and Porphyria**
C. J. WATSON. *Lancet* [*Lancet*] **1**, 539–543, March 10, 1951. 44 refs.

180. **Gaucher's Disease: a Review, and Discussion of Twenty Cases**
C. REICH, M. SEIFE, and B. J. KESSLER. *Medicine* [*Medicine, Baltimore*] **30**, 1–20, Feb., 1951. 9 figs., bibliography.

A review of Gaucher's disease and discussion of 20 cases are presented. Several distinct features were noted. Ten patients were past the age of 40; one showed no splenoheptomegaly; one had a macrocytic anaemia; pathological fractures were noted in 2; hip involvement was present in 3; and Gaucher's cell infiltration was found in the kidney of one. In 10 cases in which sternal puncture was done, Gaucher's cells were present.—[Authors' summary.]

181. **Vitamin-resistant Rickets**
H. E. PEDERSEN and H. R. MCCARROLL. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **33A**, 203–220, Jan., 1951. 5 figs., 13 refs.

Investigations were made on 25 children with a history of rickets since infancy not responding to normal doses of vitamin D: 16 of these children each had a parent similarly affected.

Treatment was begun with 300,000 units of vitamin D daily and dosage was controlled by serial plasma phosphorus and calcium estimations. It was found that a rapid rise in phosphorus and calcium levels to normal occurred, and that this was followed by radiological evidence of healing at the epiphysial line. Toxic effects, such as nausea, vomiting, and passage of calcified tubular casts in the urine, occurred only when serum calcium rose above 12 mg. per 100 ml. Alkaline phosphatase level showed a fall as healing progressed. The disease appeared to become less severe after the age of epiphysial closure, but some adults may require continued vitamin therapy. *Peter Ring*

182. **Gout. An Unusual Case with Softening and Subluxation of the First Cervical Vertebra and Splenomegaly. Result of ACTH Administration and Eventual Post-mortem Findings**
G. D. KERSLEY, L. MANDEL, and M. R. JEFFREY. *Annals of the Rheumatic Diseases* [*Ann. rheum. Dis.*] **9**, 282–304, Dec., 1950. 15 figs., 16 refs.

Details are given of the case of a man who started to have attacks of gout at the age of 18 and who died 6 years later. The unusual clinical features were splenomegaly, spontaneous partial subluxation of the first cervical vertebra due to tophaceous softening, and widespread, severe, joint affection with marked general wasting and debility. Investigations revealed persistent elevation of the plasma uric acid level (up to 17·7 mg. per 100 ml.), raised sedimentation rate, low blood cholesterol level, anaemia, and, at one stage, leucopenia.

Treatment included continuous colchicine therapy ($\frac{1}{120}$ gr. (0·8 mg.) thrice daily for 3 years), *x* irradiation, splenectomy, and adrenocorticotrophin administration. These procedures are fully discussed, with reference to reported cases.

The most notable post-mortem findings were the massive tophaceous destruction and deposition in the cervical spine, severe renal changes, marked muscle degeneration with fibrosis, and widespread amyloid deposition in the vessel walls and connective tissue of many organs. *Kathleen M. Lawther*

183. **Cortisone as an Adjunct in the Therapy of Acute Gout**
R. D. FRIEDLANDER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **145**, 11–14, Jan. 6, 1951. 11 refs.

A number of published records exist which show that adrenocorticotrophin (ACTH) together with colchicine is efficacious in terminating an acute attack of gout. Very few records of the use of cortisone for this purpose exist, however.

In this well-written paper a case is recorded of acute interval gout in which relief was both rapid and dramatic. Cortisone was not administered in this case until the usual methods of treatment had failed [but there seems to be no doubt from the author's account that relief did not occur spontaneously, but was the result of cortisone therapy].

The author puts forward his reasons for believing that cortisone may be a more effective therapeutic agent than ACTH in gout, and suggests also that it may prove in the future to be an important means of preventing this condition from progressing to the tophaceous stage. He points out that although the method by which colchicine effects relief in acute gout is unknown, there is good reason to assume that when given with cortisone or ACTH it exercises a synergistic action and prolongs remissions after the withdrawal of these substances.

W. S. C. Copeman

DIABETES

184. **The Treatment of Diabetes Mellitus.** (Лечение сахарного диабета)
A. M. GELFAND. Клиническая Медицина [*Klin. Med. Mosk.*] **28**, No. 12, 19–26, 1950.

The author has treated 800 cases of diabetes mellitus during the last 6½ years; 66% of the patients suffered in addition from arteriosclerosis, hypertension, or pulmonary tuberculosis. Of the total, 1·4% received over 100 u. insulin daily [whether soluble or PZ insulin was used is not stated], 72·6% received 60 u., and 26% 80 u. daily. As much insulin was given as was necessary for the assimilation of 80 to 83% of the carbohydrates consumed. In each individual half the caloric intake was provided as carbohydrate. The author suggests that a person weighing 60 to 70 kg. and needing 2,400 Calories daily should receive 345 g. carbohydrate, 120 g. protein, and 60 g. fat: 29·8% of patients received over 400 g. carbohydrate daily, 59·2% 300 to 400 g., and 11% 200 to 300 g. All diabetics should have one day weekly when fruit juice only should be taken; this would avoid overloading the body on the recommended "physiological diet".

N. Chatelain

185. **Diabetic Renal Disease.** [In English]
C. J. BJERKELUND. *Acta Medica Scandinavica* [*Acta med. scand.*] **139**, 133–145, Jan. 31, 1951. 3 figs., 32 refs.

The prognosis is considerably worsened when renal disease accompanies diabetes. A series of 1,335 patients with diabetes mellitus, observed in Oslo, Norway, between the years 1930 and 1950 and stabilized on insulin and dietary restrictions, serves as the basis of the present study. Albuminuria was found in 299 patients, but in 161 of these it was transient and due to intercurrent infections or disease of the urinary tract. Diabetic renal disease was found in 9% of men and 12% of women. The blood pressure of patients with renal disease was mostly higher than in patients without renal damage. Hypertension was not uncommon in diabetics over the age of 50 and was more frequent in women. With the duration of diabetes the incidence of renal disease increased and reached 31% after 15 years. Retinal lesions were noted in 132 of 923 patients examined by ophthalmologists. When renal disease was present the incidence of diabetic retinopathy was 68 to 80%, increasing with the duration of diabetes. No relationship between diabetic renal disease and body weight was established. Four typical case histories show that slight albuminuria is the earliest symptom. Granular casts are common. Pregnancy causes deterioration. At necropsy generalized arteriosclerosis is common even in young patients, and intercapillary glomerulosclerosis (Kimmelstiel–Wilson) is not uncommon.

E. Neumark

186. **Effect of Implantation of Tablets of Insulin on Normal and Alloxan-diabetic Rabbits**
I. C. GILLILAND and M. M. MARTIN. *Lancet* [*Lancet*] **1**, 143–146, Jan. 20, 1951. 3 figs., 11 refs.

Observations were made of the effect produced by the subcutaneous implantation of four types of insulin tablet on 39 normal and 25 alloxan-diabetic rabbits. Tablets of protamine zinc insulin (P.Z.I.) and cholesterol were prepared according to the method of Vargas (*Lancet*, 1949, **1**, 598); commercially prepared tablets of P.Z.I. and of neutral P.Z.I. mixed with an equal quantity of cholesterol were also used. The rabbits were rendered diabetic by giving them alloxan, 200 mg. per kg. of body weight in a 4% solution intravenously, the solution being neutralized with sodium hydroxide before use. The subsequent progress of the rabbits was assessed by estimating the body weight, the blood sugar level, the urinary excretion of sugar, and the amount of urine excreted in the 24 hours. After 4 days 2·5 to 7·5 units of P.Z.I. was injected to prevent acidosis. Both the extent of the uncontrolled glycosuria and the insulin requirements remained stable from 3 weeks after the administration of alloxan.

The P.Z.I. and cholesterol tablets produced no effect on the diabetes or other metabolic changes. Following the implantation of the P.Z.I. tablets containing 400 units of insulin an anti-diabetic effect occurred, but this lasted only 4 days and was less than that obtained from the daily injection of 2·5 units of P.Z.I. The insulin action that followed the implantation of neutral P.Z.I., either alone or mixed with an equal quantity of cholesterol, lasted only for about 2 days.

The majority of the tablets were recovered apparently intact 3 months after implantation. Their weight was comparable with unimplanted tablets, and an acid-saline extract of one of them, on injection, lowered the blood pressure dramatically. An assay showed that they contained at least 80% of their previous insulin content. Histological examination of the site from which the tablets were removed confirmed the impression that they were encapsulated. A considerable amount of foreign-body cell reaction was found around the tablets. The problem is to find a sufficiently insoluble insulin that would not be treated as a foreign body. This has not yet, however, been found possible.

R. Hodgkinson

Cardiovascular Diseases

187. **Theophylline–Ethylenediamine in the Measurement of Blood Circulation-Time**
D. N. Ross. *British Heart Journal* [*Brit. Heart J.*] **13**, 56–60, Jan., 1951. 1 fig., 14 refs.

Theophylline–ethylenediamine (" cardophylin ") was used experimentally in the measurement of the blood circulation time in normal subjects and in patients with thyrotoxicosis, anaemia, polycythaemia, and cardiovascular disease. This method, introduced by Koster and Sarnoff (*J. Lab. clin. Med.*, 1943, **28**, 812) was chosen because of the easily recognizable objective end-point—an inspiratory gasp or, less often, swallowing movements or change in expression after the rapid intravenous injection of 1 ml. (containing 0·24 g. of cardophylin). Trials involving 432 tests in 337 subjects are described and the results clearly tabulated. It is stated that in no case was there any dangerous reaction, and that most of the subjects investigated " spoke of a feeling of warmth and of light-headedness lasting for about half a minute "; in 8 psychoneurotic patients, however, the injection produced " a violent emotional upset, with weeping, trembling, and tachycardia ". Leakage of the solution around the vein may produce pain, but necrosis or thrombosis never occurred.

The mean circulation time in 150 normal subjects, each tested once only, was 12·1 seconds (range 6·8 to 22·0 seconds). The findings in patients with various pathological conditions were as follows:

Condition	No. of Tests	Circulation Time in Seconds	
		Range of Readings	Mean
Anaemia	39	6·0–15·9	9·2
Polycythaemia	2	17·6–19·0	18·3
Thyrotoxicosis:			
Untreated	18	5·6–13·6	7·1
Treated	15	10·0–17·4	14·0
Hypertension without cardiac failure ..	9	10·0–17·0	12·8
Valvular disease without cardiac failure ..	23	6·2–16·4	12·4
Rheumatic carditis	11	7·6–17·0	10·4
Cardiac failure:			
(*a*) Left ventricular ..	25	15·8–35·0	21·0
(*b*) Right ventricular ..	40	13·0–58·0	21·0

On the whole these results agree with those obtained with Fishberg's saccharin method. The author claims that the theophylline–ethylenediamine test is safe, simple, reliable, and suitable for routine use.

[The cardophylin test should certainly be of great help when the cooperation of the patient cannot be obtained to perform the " decholin " or saccharin test. It could also be used to confirm the circulation time as found by one of the two other methods. Cardophylin is a safe drug, but the abstracter has seen unpleasant side-effects (vomiting, collapse, perspiration) during intravenous administration of this substance on two occasions; both patients were in status asthmaticus and the drug, in the usual dosage, was given for therapeutic purposes.] *A. I. Suchett-Kaye*

ELECTROCARDIOGRAPHY

188. **The Ventricular Complex in Esophageal Electrocardiography**
L. Scherlis, J. Wener, A. Grishman, and A. A. Sandberg. *American Heart Journal* [*Amer. Heart J.*] **41**, 246–265, Feb., 1951. 11 figs., 28 refs.

Electrocardiographic patterns obtained from multiple oesophageal leads were studied in 85 patients, including 15 in whom a diagnosis of posterior myocardial infarction had been made from the history and clinical course and the presence of abnormal Q waves in V_F. The leads were spaced at intervals of 1·75 cm. and extended from 6 cm. below the level of the diaphragm to supracardiac levels. In all the patients with posterior myocardial infarction the pattern obtained in V_F was duplicated in the lower oesophageal leads, and in 13 of them the Q wave persisted in all the oesophageal leads up to and including those at ventricular and atrial levels. In 2 the abnormal Q wave was replaced by a qR or R pattern at higher levels. In a further 5 patients with borderline abnormal Q waves in V_F, similar patterns were obtained in the lower oesophageal leads, which were therefore of no help in diagnosis. Although there is a definite transition zone in which the electrocardiographic pattern changes from that recording ventricular surface activity to that recording left ventricular cavity potential, there is considerable variation in the level of occurrence of this change, and of the appearance of atrial intrinsic deflections.

[This carefully documented article should be read in its entirety as it is impossible to do justice to it in a brief abstract. It marks a definite advance in oesophageal electrocardiography, but also clearly indicates the need for much further work before accurate clinical use can be made of it.] *William A. R. Thomson*

189. **The Effect of Pneumoperitoneum on the Electrocardiogram. A Study of the Results Obtained with Standard and Unipolar Leads**
A. Pollak. *Diseases of the Chest* [*Dis. Chest*] **19**, 36–57, Jan., 1951. 3 figs., 24 refs.

Electrocardiograms (standard limb leads, the CF leads, the three augmented unipolar limb leads, and the V leads) were recorded in the recumbent and the sitting positions in 19 unselected tuberculous patients receiving pneumoperitoneum treatment. Eight of the patients had had right phrenic interruption and 3 had had left phrenic

interruption. In the recumbent position practically all the electrocardiograms were within normal limits without axis deviation. In the sitting position standard leads showed a left axis shift in the majority, with a deep Q_3 occurring not uncommonly, while the unipolar lead electrocardiograms showed a change to a more horizontal position of the heart. No important difference was noted between the results obtained with the standard limb and the unipolar lead records, which produced parallel, if not identical, results. Frequent T changes were noted, especially in the sitting position, including frequent inversion of T_3 and occasional inversion of T in CF_4, I, V_3, and V_4. Fluoroscopy showed that the axis shift recorded in the sitting position could not be due to elevation of the diaphragm, and it is concluded that it is due to counterclockwise rotation of the heart. In the recumbent position deep inspiration had no effect upon the electrocardiogram in patients who had not had a phrenic crush. In the sitting position the effects were more marked in such patients: increase in height of R_3, diminution of Q_3 and S_3, and changes in T_3. Comparable changes were recorded in aV_F (the only other lead used in investigating the effect of inspiration), particularly increase in the height of R. *William A. R. Thomson*

190. **Electrocardiographic Abnormalities Induced by Cardiac Catheterization**
R. P. Lasser, R. Borun, A. J. Gordon, and F. H. King. *Journal of the Mount Sinai Hospital* [*J. Mt. Sinai Hosp.*] **17**, 295–302, Jan.–Feb., 1951. 4 figs., 15 refs.

Of a number [unstated] of electrocardiograms recorded during cardiac catheterization, 49 were selected for analysis on account of induced abnormalities of rhythm or conduction. Auricular, nodal, and ventricular ectopic beats were noted frequently. Paroxysmal tachycardia, supraventricular or ventricular, was not uncommon. Partial A-V block was observed in one case, incomplete bundle-branch block in 5 cases, and complete bundle-branch block in 3. The ectopic rhythm ceased as soon as the catheter tip was removed from the excitable area in all these cases except one, a case of Wolff–Parkinson–White syndrome in which auricular tachycardia persisted for 5 hours. Of the cases with disturbance of conduction, in 5 it was still present at the end of the procedure, but disappeared within a day or two. *Paul Wood*

191. **The Natural History of the Electrocardiogram in Mitral Stenosis.** [In English]
H. Rasmussen and J. Boe. *Cardiologia* [*Cardiologia, Basel*] **18**, 33–44, 1951. 9 figs., 7 refs.

Serial electrocardiograms (standard limb leads) were recorded in a series of 50 patients with mitral stenosis over periods ranging from 1 to 18 years (average 6 years). The findings confirmed the presence in such patients of the " characteristic, but not specific, electrocardiographic changes " which the senior author has reported in previous papers. In 18 cases they observed the development in lead I of a low R, a broad-based straddling R, notching of R, or a second small wave following the main R wave. In 11 cases right axis deviation developed, while in 7 a right ventricular retardation (type I) developed. In attempting to correlate the presence of these changes with the size of the heart, it was noted that of 17 patients in whom there was considerable increase in size of the heart, 15 had electrocardiographic changes, whilst of 18 patients in whom there was no increase in size of the heart, 12 had electrocardiographic changes. Attention is drawn to the fact that the changes in the electrocardiogram were most irregular in time. For 10 years or more no changes might be noted, then within a matter of months marked changes would occur. This is taken to be an argument in favour of the view that dilatation rather than hypertrophy of the right ventricle is the main factor responsible for the electrocardiographic changes. Six unipolar precordial leads were used in the final records taken on all 50 patients, and showed relatively few significant changes compared with the limb leads. When first observed, 21 of the patients had sinus rhythm, compared with only 9 at the final examination. The corresponding figures for persistent auricular fibrillation were 24 and 39.
William A. R. Thomson

192. **$Q–T_C$ Interval of the Electrocardiogram in Acute Rheumatic Carditis in Children**
N. H. Solomon and M. Zimmerman. *American Journal of Diseases of Children* [*Amer. J. Dis. Child.*] **81**, 52–58, Jan., 1951. 3 figs., 9 refs.

The authors determined the $Q–T_C$ (Q–T interval corrected for cardiac rate) by Bazett's formula in 27 children with acute rheumatism, all but 2 having evidence of carditis, and in 25 controls. They regard 0·422 sec. as a satisfactory figure for the upper limit of normal, as in 23 of the 25 controls the value of $Q–T_C$ was below this. Of the 25 patients with active carditis, in 21 the $Q–T_C$ was above 0·422 sec. on at least one occasion. A persistently increased $Q–T_C$ is considered by the authors to indicate a continually active carditis and to be of corresponding prognostic value [although the supporting evidence given is not convincing].
J. A. Cosh

193. **A Universal Deviometer and the Value of Deviometry in Assessing the Functional State of the Myocardium.** (Универсальный девиометр и значение девиометрии в оценке функционального состояния миокарда)
L. N. Goldman and V. E. Merkul. Клиническая Медицина [*Klin. Med., Mosk.*] No. 1, 80–84, 1951. 4 figs., 3 refs.

The authors describe an instrument which they have devised whereby the deviation of the electrical axis of the heart, and also of each separate wave of the electrocardiographic complex, may be simply and rapidly calculated from the height of the wave concerned. [For details the original should be consulted.]

They discuss the value of such measurements in diagnosis and prognosis, and cite as an example a case of myocardial infarction in which the deviation of the T wave was 131 degrees. After 2 months, when the patient's condition had considerably improved, the deviation was 30 degrees. The corresponding deviations

of the electrical axis of the heart were 137 and 14 degrees respectively. In a case where the inclination of T was 150 degrees and that of the heart axis 300 degrees the patient died in 2 months. In infarcts of the posterior wall the inclination was normal in 8 cases and negative in 17. In those of the anterior wall 17 were normal, 3 positive, and 10 negative. In those of the antero-posterior type the inclination was normal in 6 cases and negative in 3. The deviation of T from the heart axis was high, which corresponded to the grave condition of these patients. While the deviation of the T wave is the most informative, it is equally easy to calculate that of the Q or S wave. *L. Firman-Edwards*

HEART

194. **Determinants of Impairment of Cardiac Filling during Progressive Pericardial Effusion**
W. E. NERLICH. *Circulation* [*Circulation*] **3**, 377–383, March, 1951. 3 figs., 10 refs.

It was the purpose of this investigation to subject the accepted dynamics of pericardial effusion to closer scrutiny. The right and left atrial and pericardial pressures were recorded in anaesthetized animals by means of cannulae attached to optical manometers, and a progressively increasing quantity of saline injected into the pericardial sac. Evaluation of changes in instantaneous pressures in the right and left auricles at the end of ventricular diastole and at the end of systole indicate that the following changes occur with a progressive rise in pericardial pressure: (1) diminution in auricular and ventricular diastolic capacities; (2) increase in intra-auricular pressures (more marked on the left side owing to the higher elasticity coefficient of this auricle), with corresponding decrease in veno-atrial pressure gradient; (3) blockage of auricular inflow during ventricular diastole (due to rise in intrapericardial pressure); (4) impairment of auricular filling during ventricular systole as the stroke volume diminishes to an extreme degree; and (5) inauguration of a vicious circle in which a diminishing veno-atrial pressure gradient decreases ventricular filling and the lessened systolic contraction of the ventricle no longer exerts its salutary effect on pericardial and intra-atrial pressures. *T. Semple*

195. **Further Experiences with Microplethysmography in the Study of Congenital Heart Disease**
R. S. MEGIBOW and S. FEITELBERG. *Journal of the Mount Sinai Hospital* [*J. Mt Sinai Hosp.*] **17**, 303–309, Jan.–Feb., 1951. 5 figs., 3 refs.

The microplethysmograph was used to record changes in digital volume during the cardiac cycle. The curve normally shows a steep ascent in systole, a sharp peak, and a slower descent interrupted by a faint dicrotic notch. In conditions such as patent ductus arteriosus the peak is rounded, the descending limb steeper, and the dicrotic notch is lost. The authors claim that microplethysmography offers a useful and valuable diagnostic tool for the evaluation of certain congenital cardiac defects. *Paul Wood*

196. **Treatment of Chronic Congestive Cardiac Failure with Ion Exchange Resins**
E. E. KLEIBER and G. PICKAR. *Annals of Internal Medicine* [*Ann. intern. Med.*] **34**, 407–414, Feb., 1951. 3 figs., 4 refs.

It is now well established that sodium retention is an important feature of congestive cardiac failure with oedema. Elimination of salt from the body by mercurial diuretics and by low-salt diet has taken an important therapeutic place. Carboxylic resins are available which will hold sodium in the intestine. This enables the patient to take a more or less normal diet, the sodium content of which will not be fully absorbed. In 3 patients the results of giving such resins was striking, but in 4 other patients the drug caused severe gastro-intestinal discomfort and was refused. The resin used was somewhat bulky and of a sandy consistency. About half an ounce (15·5 g.) had to be taken three times a day.

The authors give the following warnings: (1) Decreased absorption of base may lead to an acidosis; this is a special danger if the kidneys are damaged and are unable to form ammonia. (2) Some resins may deplete the body of other mineral substances, such as potassium and calcium; this may be averted by the administration of additional calcium or potassium salts. (3) Only about half the patients will consent to take these resins. *J. McMichael*

197. **An Intracardiac Manometer: its Evaluation and Application**
E. J. ELLIS, O. H. GAUER, and E. H. WOOD. *Circulation* [*Circulation*] **3**, 390–398, March, 1951. 10 figs., 16 refs.

See also Section Pathology, Abstract 120.

198. **Penicillin-resistant Subacute Bacterial Endocarditis Treated by a Combination of Penicillin and Streptomycin**
J. E. CATES, R. V. CHRISTIE, and L. P. GARROD. *British Medical Journal* [*Brit. med. J.*] **1**, 653–656, March 31, 1951. 28 refs.

Four cases of subacute bacterial endocarditis are described which were due to penicillin-resistant organisms: 3 to *Streptococcus faecalis* and 1 to *Streptococcus viridans*. In 2 cases courses of streptomycin and of aureomycin were given, and in a third chloramphenicol, all without success. The combination of penicillin with aureomycin was equally unsuccessful. Following the work of Hunter (*Amer. J. Med.*, 1946, **1**, 83; 1947, **2**, 436) the authors gave a combination of 20 mega units of penicillin and 4 g. of streptomycin daily for at least 6 weeks (except in one case in which the patient died from heart failure after myocardial infarction 5 days after the beginning of treatment). The 3 other patients survived: one died from congestive heart failure 17 days after the end of treatment, in the two others severe vestibular damage remained. Laboratory tests showed an additive effect of streptomycin and penicillin, and on the other hand a retardation of the bactericidal effect of penicillin by the addition of aureomycin. [These

observations show that the combination of these two antibiotics may be life-saving, but at the same time emphasize the risk of severe vestibular damage.]

A. Schott

199. **Subacute Bacterial Endocarditis due to *H. parainfluenzae* and *Str. viridans***
J. G. GOUDIE and C. P. LOWTHER. *British Medical Journal* [*Brit. med. J.*] **1**, 217–218, Feb. 3, 1951. 13 refs.

DISTURBANCES OF RHYTHM

200. **Thiouracil Compounds in the Prevention of Paroxysmal Cardiac Arrhythmia**
H. D. RUSKIN. *Lancet* [*Lancet*] **1**, 134–137, Jan. 20, 1951. 9 refs.

Methyl and/or propylthiouracil in a daily dosage of 0·6 g. divided in three parts was given to 7 patients suffering from paroxysmal cardiac arrhythmia. Two patients had apparently normal hearts, 3 had hypertensive heart disease, and 2 had rheumatic valvular disease. None showed evidence of thyrotoxicosis. Electrocardiographic proof of the arrhythmia was obtained in 6 cases; 3 patients had supraventricular tachycardia, 2 auricular flutter with auriculo-ventricular block, and 2 auricular fibrillation. In 4 the paroxysms were completely prevented, in 2 they became less frequent, and in 1 who was also suffering from valvular heart disease of rheumatic origin with gross cardiac enlargement there was no response.

Of the 7 patients, 6 had failed to respond to quinidine. The rapidity of the response of some patients suffering from angina pectoris and paroxysmal arrhythmia to treatment with thiouracil compounds, and their relapse when the drug was discontinued, suggested a similar mode of action in both conditions. Possibly the myocardium was the site of the action. In the patients responding to treatment the drug was effective within a week. In 2 patients the combination of quinidine with a thiouracil compound was more effective than either drug alone.

R. Hodgkinson

201. **Critical Rates in Ventricular Conduction. Simulation of Ventricular Tachycardia**
H. VESELL and L. B. KRAEMER. *American Heart Journal* [*Amer. Heart J.*] **41**, 280–290, Feb., 1951. 5 figs., 13 refs.

The authors describe 5 cases in which a bundle-branch block was associated with tachycardia, and simulated ventricular tachycardia. The effect is attributed to the inability of a diseased bundle to transmit impulses sufficiently rapidly. *R. T. Grant*

202. **Paroxysmal Nodal Tachycardia with Retrograde Heart Block**
J. A. COSH. *British Heart Journal* [*Brit. Heart J.*] **13**, 74–79, Jan., 1951. 7 figs., 15 refs.

A case of "low nodal" paroxysmal tachycardia with delayed retrograde conduction is reported in a girl of 11, not apparently suffering from organic heart disease. The attack lasted probably 10 days, and for the last 4 days the patient was treated with quinidine sulphate, 8 grains (0·52 g.) on the first day, increasing to 20 grains (1·3 g.) on the third day, in divided doses. Vagal stimulation (pressure on the eyeballs) on the seventh day of the tachycardia prolonged the R–T interval from 0·14 to 0·20 second, when an auricular beat was dropped. About 12 hours before the end of the paroxysmal attack, spontaneous retrograde block was observed, with predominantly 3 : 2 ventriculo-atrial rhythm. Other interesting points were that during the period of observation the ventricular rate gradually slowed from 195 to 158 a minute; that dilatation of the heart was found during the attack, but normal size was observed on the fourth day after the paroxysm; and that temporary inversion and broadening of the T waves was seen after the attack, causing lengthening of the duration of electrical systole as determined by Bazett's formula (K being 0·51 instead of the normal 0·37 to 0·40).

A. I. Suchett-Kaye

203. **Disorders of the Cardiovascular System Occurring with Catheterization of the Right Side of the Heart**
W. T. ZIMDAHL. *American Heart Journal* [*Amer. Heart J.*] **41**, 204–216, Feb., 1951. 3 figs., 24 refs.

The author reviews the published accounts of complications following cardiac catheterization and describes two further cases. One patient developed a nodal tachycardia during catheterization. Normal rhythm was restored by the injection of 2 ml. of 2% procaine into the superior vena cava through the catheter. The second patient (Fallot's tetralogy) developed complete A-V heart block one day after removal of the catheter. Normal rhythm returned after one week.

R. T. Grant

204 (*a*). **Auricular Flutter.** (Flutter auriculaire)
M. R. HEJTMANCIK, G. R. HERRMANN, and J. Y. BRADFIELD. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **44**, 16–23, Jan., 1951. 22 refs.

A series of 93 bouts of auricular flutter recorded in 82 patients are reviewed. Age and sex incidence, types of underlying heart disease, and precipitating factors are listed in tabular form. According to whether the arrhythmia lasted for longer or less than 72 hours, the condition was arbitrarily divided into established (50) and transient (32). The auricular rate varied between 210 and 374 per minute. Five patients had 1 : 1 auriculo-ventricular (A-V) conduction; in 46 the ventricular rhythm was regular because of constant A-V block. *A. Schott*

204 (*b*). **Auricular Flutter.** (Flutter auriculaire)
G. R. HERRMANN and M. R. HEJTMANCIK. *Archives des Maladies du Cœur et des Vaisseaux* [*Arch. Mal. Cœur*] **44**, 23–34, Jan., 1951. 1 fig., 23 refs.

Results of treatment of 28 attacks of transient flutter in 24 patients, and of 55 attacks of established flutter in 48 patients, are discussed. Out of 29 cases digitalis restored sinus rhythm directly in 3, and converted flutter

into fibrillation in 18. In 14 of these sinus rhythm was restored on discontinuing digitalis; in 4 quinidine had to be given in addition. Quinidine proved effective, particularly in flutter of short duration. In one case it produced 1 : 1 conduction with collapse. The combination of quinidine and digitalis given together was less effective, but is recommended in cases of flutter complicating myocardial infarction and in instances in which quinidine alone produces 1 : 1 conduction. The prophylactic use of quinidine, potassium, and digitalis is briefly discussed. *A. Schott*

205 (*a*). **Transient Right Bundle Branch Block Produced by Heart Catheterization in Man**
E. SIMONSON. *American Heart Journal* [*Amer. Heart J.*] **41**, 217–224, Feb., 1951. 5 figs., 14 refs.

Cardiac catheterization in a patient with mitral stenosis caused right bundle-branch block lasting for one hour. Recovery in this case was spontaneous.
R. T. Grant

205 (*b*). **Prognosis in Bundle Branch Block. II. Factors Influencing the Survival Period in Left Bundle Branch Block**
R. P. JOHNSON, A. L. MESSER, —. SHREENIVAS, and P. D. WHITE. *American Heart Journal* [*Amer. Heart J.*] **41**, 225–238, Feb., 1951. 1 ref.

A consecutive series of 555 patients with left bundle-branch block is presented. The average survival period for the group was 3·3 years, and 4·9 years for those who survived the first year. A detailed analysis shows a better survival in young patients, women, those with a short QRS duration (except those in whom it was very short—0·12 second), those with no cardiac enlargement, and those without evidence of coronary disease.
D. Verel

VALVULAR DISEASE

206. **Diagnosis of Aortic Stenosis Based on a Study of 25 Proved Cases**
D. LEWES. *British Medical Journal* [*Brit. med. J.*] **1**, 211–216, Feb. 3, 1951. 25 refs.

In 2,245 routine necropsies 45 (1·8%) cases of aortic stenosis were found, and in 25 of these the calcareous lesion was confined to the aortic valve. The author suggests that incorrect appreciation of the history and physical signs may frequently lead to this condition being overlooked during life. In just over half the cases in this series the clinical diagnosis was made correctly; it usually related to the severity of the valvular stenosis. Characteristic symptoms were lassitude, giddiness, angina, and syncope. Most patients died within 18 months of the onset of first symptoms from left heart failure, often of a form peculiarly resistant to treatment. In several cases attacks of sweating, pallor, or mental confusion occurred in the terminal stages, and in 4 infective endocarditis developed. Valuable diagnostic signs were a harsh aortic systolic murmur and radioscopically visible calcified aortic valves. The classical signs of a slowly rising pulse, a large left ventricle, an aortic systolic murmur and thrill, and an absent second sound were often unreliable in this series of 25 cases in which there was proved calcareous aortic stenosis.
J. L. Lovibond

207. **Mural Thrombosis and Arterial Embolism in Mitral Stenosis. A Clinico-pathologic Study of Fifty-one Cases**
R. A. JORDAN, C. H. SCHEIFLEY, and J. E. EDWARDS. *Circulation* [*Circulation*] **3**, 363–367, March, 1951. 1 fig., 14 refs.

Out of 11,536 necropsies performed at the Mayo Clinic during the 20-year period 1929 to 1948 there were 51 cases of mitral stenosis with intracardiac mural thrombi. Of the 42 cases in which mural thrombi were present in the left side of the heart (including 15 in which the right side was also involved), they were restricted to the auricular appendage in only 20. It would seem, therefore, that surgical resection of the left auricular appendix in such patients would offer no more than a 50% chance of eliminating the source of systemic arterial emboli. On the other hand, right atrial thrombi were restricted to the auricular appendix in 20 out of 24 cases, but embolism from thrombi in peripheral veins would still have to be reckoned with when considering surgical resection or obliteration of this appendix for repeated pulmonary infarction. *T. Semple*

208. **Studies of the Circulatory Dynamics in Mitral Stenosis. II. Altered Dynamics at Rest**
R. GORLIN, F. W. HAYNES, W. T. GOODALE, C. G. SAWYER, J. W. DOW, and L. DEXTER. *American Heart Journal* [*Amer. Heart J.*] **41**, 30–45, Jan., 1951. 5 figs., 32 refs.

The effect of mitral stenosis on the pulmonary circulation of 21 patients with mitral stenosis was observed. Many of the patients were seriously affected, and 6 were so affected that they had physical signs of pulmonary oedema. As a result of the obstruction caused by the stenosed valve the cardiac output was reduced. Fibrillation of the auricles appeared to reduce the output still further. Behind the stenosis, both in the small pulmonary vessels and in the pulmonary artery, the pressure was increased. When pulmonary "capillary" pressure rose to around 25 mm. Hg, the pulmonary arteriolar resistance began to rise sharply. In all cases the pulmonary arteriolar resistance was increased and the increase was roughly related to the elevation of the pulmonary capillary pressure and the degree of valvular stenosis.

One effect of the increase in pulmonary vascular resistance was to increase the work of the right ventricle greatly. Failure of the right ventricle to sustain this increased work was indicated by an elevated ventricular filling pressure. Such "failure" was seen in more than half of the patients studied. The stroke output per square metre was calculated in each case and found, when plotted logarithmically, to vary inversely with the total pulmonary resistance. *H. E. Holling*

209. **Effects of Exercise on Circulatory Dynamics in Mitral Stenosis. III**
R. GORLIN, C. G. SAWYER, F. W. HAYNES, W. T. GOODALE, and L. DEXTER. *American Heart Journal* [*Amer. Heart J.*] **41**, 192–203, Feb., 1951. 3 figs., 19 refs.

The authors report 9 observations on 8 cases of mitral stenosis with minimal disease of other valves. All but the most severe clinical grades of stenosis were represented, only patients thought to be unable to exercise safely being excluded. Despite this selection, 3 patients developed pulmonary oedema during the investigation.

Pulmonary "capillary" pressure was recorded at rest, and then during exercise performed (while recumbent) on a bicycle ergometer. After recovery, pulmonary and brachial arterial pressures were simultaneously measured at rest and during exercise, and the cardiac output estimated by the direct Fick method. Exercise increased the oxygen consumption to 1·5 to 3 times the resting level. In 8 observations there was no change in arterial oxygen saturation, and in the 5 patients with a low fixed cardiac output there was a proportional increase in arterio-venous oxygen difference. The mean resting pulmonary "capillary" pressure was raised in all cases and further increased with exercise. The pulmonary arterial pressure rose with the pulmonary "capillary" pressure, and the "PA–PC" gradient was unchanged, or rose only 1 to 15 mm. Hg. The calculated pulmonary arteriolar resistance was unchanged by exercise in 2 cases, and rose in 2 cases. In 5 out of 6 cases the pulmonary artery and pulmonary "capillary" pulses and pressures had returned to normal by 2 or 5 minutes after exercise.

The authors suggest that cardiac output becomes fixed in mitral stenosis because of: (1) the very high pulmonary arteriolar resistance, (2) the limitation of the patient's effort by pulmonary congestion, and (3) the decrease in stroke volume of the right ventricle resulting from the fixed output and the tachycardia on exercise. Three patients were orthopnoeic at rest and had high resting pulmonary "capillary" pressures (26 to 34 mm. Hg). On exercise these patients developed pulmonary oedema, with a rise in pulmonary "capillary" pressure to 35 to 47 mm. Hg. In other cases, in which the resting value was lower, no oedema developed despite a rise above 35 mm. Hg on exercise. *D. Verel*

210. **The Diagnosis of Tricuspid Stenosis.** (El diagnostico de la estenosis tricuspidea)
J. M. RIVERO-CARVALLO. *Revista Española de Cardiología* [*Rev. esp. Cardiol.*] **4**, 497–506, Nov.–Dec., 1950. 3 figs., 6 refs.

In a brief study of the literature it is stated that tricuspid stenosis is found in about 10% of cases of rheumatic heart disease. It is always associated with tricuspid incompetence. The author describes the effect of post-inspiratory apnoea on the auscultatory signs of tricuspid disease, the diastolic murmur, the "snap" of the opening valve, and the systolic murmur being made more obvious by an increase in intensity and roughness during apnoea, whereas aortic and mitral murmurs become less audible during this period. It is stressed that the tricuspid zone is usually distant from its classical position, and may be found anywhere along the left border of the lower sternum toward the apex area. This is attributed to rotation of the heart.
J. J. Giraldi

CORONARY ARTERY DISEASE

211. **Arteriolar Disease of the Heart**
S. A. JACOBSON and T. J. RANKIN. *Angiology* [*Angiology*] **1**, 474–483, Dec., 1950. 2 figs., 26 refs.

A case with clinical evidence of cerebral and cardiac ischaemia is described. A necropsy, which unfortunately did not include the brain, revealed a macroscopically normal heart without evidence of coronary artery disease. Histological examination showed coronary arteriolosclerosis; the findings are compared with those in 2 other cases in the literature. The rarity of the condition is emphasized, the literature is discussed, and a theory is proposed to explain the infrequency of arteriolar disease of the heart.

[This is an unsatisfactory paper in that although the discussion of the literature is very lengthy, the histological details and investigation of this case appear to be incomplete.] *G. J. Cunningham*

212. **Comparison of Clinical and Pathologic Aspects of Coronary Artery Disease in Men of Various Age Groups: a Study of 950 Autopsied Cases from the Armed Forces Institute of Pathology**
W. M. YATES, P. P. WELSH, J. F. STAPLETON, and M. L. CLARK. *Annals of Internal Medicine* [*Ann. intern. Med.*] **34**, 352–392, Feb., 1951. 6 refs.

The clinical and necropsy findings in 950 cases of coronary artery disease from the records of the U.S. Armed Forces Institute of Pathology are analysed with special reference to age grouping: 47% of the cases occurred under the age of 40, and 12% under the age of 30 years. Owing to the mode of selection of the data this is not to be taken as an over-all incidence in the population. White were more liable to coronary thrombosis than negro soldiers. Hypertension did not appear to be an important factor in the under-40 group. The coronary attack came on more frequently during strenuous activity in the young group, while over the age of 40 there was a higher incidence of premonitory symptoms or previous manifestations of coronary artery disease. The first attack was more frequently fatal in men under 40. Myocardial scarring increased with age, and congestive failure from ischaemic heart disease was commoner in the older group. Rhythm and conduction disturbances in the electrocardiogram increased with age. Thrombotic occlusion of the coronary vessels was the rule in the under-40 group, while over this age arteriosclerotic narrowing complicated the picture. Mural thrombi, myocardial fibrosis, ventricular aneurysm, and pericarditis in association with recent infarction were all found with greater frequency with advancing age. Non-cardiac infarcts also increased with advancing

years. The majority of subjects with pulmonary infarcts did not have mural thrombi on the right side of the heart. In general, the prognosis of coronary artery disease under the age of 40 would appear to be worse than in men aged 40 and over. *J. McMichael*

213. **Cardiac Aneurysm: Clinical and Electrocardiographic Analysis**
J. B. MOYER and G. I. HILLER. *American Heart Journal* [*Amer. Heart J.*] **41**, 340–358, March, 1951. 4 figs., 39 refs.

This concise review of the literature of cardiac aneurysm and account of 20 cases (12 with necropsy control) is chiefly concerned with the electrocardiographic (ECG) findings. The authors suggest that there is no pattern characteristic of ventricular aneurysm. ECG changes, when present, are those of antecedent extensive myocardial infarction. Persistent RS–T elevation is present in many cases, but the authors agree with others that this may be found with large infarcts in the absence of aneurysm formation. It is probably due to hypertrophy of the opposite heart wall, the ECG changes resulting from this being transmitted through the destroyed myocardium. An upright R wave in lead aVR is not an invariable finding. *A. Venner*

See also Section Pathology, Abstracts 124–5, and 142.

DISORDERS OF CIRCULATION

214. **The Dihydrogenated Ergot Alkaloids in the Treatment of Essential Hypertension**
F. R. NUZUM. *Annals of Western Medicine and Surgery* [*Ann. west. Med. Surg.*] **4**, 781–788, Dec., 1950. 10 figs., 24 refs.

Among the alkaloids of ergot are ergokryptine, ergocornine, and ergocristine. The hydrogenated compounds of these alkaloids have been found to have almost no constrictor action on smooth muscle, but to inhibit the sympathetic system; they are available as dihydroergocornine (" DHO 180 "), dihydroergokryptine " DHK 135 "), and a mixture of these two with dihydroergocristine (" CCK 179 "). A series of 32 patients with hypertension were given one or other of these compounds by mouth or intramuscularly; 10 of these cases are reported. In some there was an initial fall in blood pressure, especially after injections, but in all cases the pressure had returned to the original level before the course had ended. *C. W. C. Bain*

215. **Therapy of Hypertension. The Use of Veratrum Viride Alone and Combined with Certain Dihydrogenated Alkaloids of Ergot**
I. L. JOSEPHS. *Annals of Western Medicine and Surgery* [*Ann. west. Med. Surg.*] **4**, 789–794, Dec., 1950. 29 refs.

Veratrum viride contains several alkaloids and acts as a vagotonic. Injection into animals causes a slowing of respiration and of the pulse, and a fall in blood pressure. In man the drug is given by mouth, dosage being measured in " craw units ", one unit being the minimum lethal dose for this small crustacean. To 25 patients with essential hypertension a test dose of 10 units of veratrum viride was given, after which the optimum daily dose was determined. This varied from 20 to 40 units, taken after breakfast. Toxic reactions included pain in the chest and epigastrium and diarrhoea. On account of these reactions only 4 of the 25 patients were able to tolerate a large enough dose of the drug to cause a fall in the diastolic pressure of more than 10 mm. Hg. Of the remaining patients, 10 were then given, in addition, 2 to 5 mg. of " CCK 179 " (a mixture of the three sympathicolytic alkaloids of ergot) which they had previously been unable to take except for short periods or in inadequate doses owing to its " blocking effect ". Good results are claimed from this combined therapy, falls in blood pressure of up to 70 mm. Hg systolic and 30 mm. Hg diastolic being recorded and maintained up to 10 months. The remaining 11 patients were found to respond to CCK 179 alone, equally good results being noted. *C. W. C. Bain*

216. **The Effect of the Dihydrogenated Ergot Alkaloids (CCK–179) on the Electrocardiogram**
M. C. THORNER, C. T. STOLPESTAD, and G. C. GRIFFITH. *Annals of Western Medicine and Surgery* [*Ann. west. Med. Surg.*] **4**, 795–798, Dec., 1950. 3 figs., 11 refs.

Five patients with normal blood pressure and 5 with hypertension were given intravenous injections of " CCK 179 " (a mixture of the 3 sympathicolytic dihydrogenated ergot alkaloids). Electrocardiograms were taken 5 to 60 minutes after the injections. No changes were found, although substantial falls in blood pressure were noted in 2 of the patients.
C. W. C. Bain

217. **The Lack of Effect of Oral Doses of Cinchona Alkaloids on the Circulation of Dogs with Renal Hypertension. A Contrast to their Action in Neurogenic Hypertension**
I. GREENE and E. P. HIATT. *Circulation* [*Circulation*] **3**, 399–404, March, 1951. 3 figs., 16 refs.

218. **Postural Hypotension: the Localization of the Lesion**
D. VEREL. *British Heart Journal* [*Brit. Heart J.*] **13**, 61–67, Jan., 1951. 1 fig., 20 refs.

Three cases of so-called idiopathic postural hypotension were investigated and experimental findings bearing on the location of the lesion are reported in this paper. Fainting attacks occurred in all cases as a result of a great fall in blood pressure when assuming the standing position. The mechanism of these fainting attacks is apparently quite different from that operating in ordinary fainting, in which the muscle blood flow increases as the blood pressure falls. No such increase in muscle blood flow from vasodilatation in muscle was observed in postural hypotension. The association in this condition of disturbances in the regulation of blood pressure, pulse rate, sweating (anhidrosis), and sexual function points to the autonomic nervous system as the

mediator of the phenomena. Furthermore, the experimental findings in these cases and in others reported in the literature provide strong evidence that the syndrome is due to a central failure of the carotid reflex.

A. I. Suchett-Kaye

219. **Pathogenesis of Arterial Hypotension.** (К патогенезу артериальной гипотонии)
A. S. KOBIZEV. Советская медицина [*Sovetsk. Med.*] No. 1, 18–20, 1951.

The author has made a study of 180 cases of arterial hypotension during the past 5 years. In most cases the arterial hypotension was secondary to some other illness (gastric ulcer, duodenal ulcer, heart disease, myxoedema). Insufficient nutrition was thought to be the main cause of essential or primary hypotension during the war years. Among 42 cases of hypotension observed during the war there were 30 cases of primary or essential hypotension. In 1949 there were 14 cases of primary hypotension among 30 cases observed. In 20 cases of primary hypotension and 20 of secondary hypotension the haemodynamics was investigated. In the former a low arterial tension was often combined with a low venous tension, and in most cases a reduction in blood volume was noted (Congo-red and calorimetric tests). The blood circulation time appeared to be normal by the ether and calcium chloride tests. Investigation of the capillaries showed them to be well developed, often dilated, and elongated, the blood flow being slowed down.

In all the 20 cases of secondary hypotension there was a normal venous tension; the volume of the circulating blood was normal or a little below normal, the blood circulation time was variable, and the capillaries were normal except in cases of heart disease. The reason for a reduction in the blood volume in primary hypotension is thought to lie in a dilatation of the venous capillaries, with slowing of the blood flow and a reduction in venous pressure. In these cases drugs which raise the venous pressure are recommended (camphor, leptazol, strychnine). In secondary hypotension, without low venous pressure, the primary cardiac cause should be attended to, and ephedrine may be found to be of use. *N. Chatelain*

BLOOD VESSELS

220. **The Treatment of Obliterative Endarteritis with Sex Hormones.** (Лечение облитерируюшего эндартериита модовыми гормонами)
Z. L. GORDON. Клиническая Медицина [*Klin. Med. Mosk.*] **28**, No. 12, 48–52, 1950. 4 refs.

The therapeutic effect of sex hormones on the vascular, especially the arterial, system was studied by the author, 50 in-patients and 32 out-patients being thus treated. Of the 82 patients 5 were women and 50 had a history of endarteritis for over 4 years. Age distribution was: 20 to 30 years, 7 patients; 31 to 40 years, 15 patients; 41 to 50 years, 46 patients; 51 to 60 years, 12 patients; and over 60 years, 2 patients. Endarteritis in one upper or lower limb was present in 36 cases, both upper or lower limbs in 40 cases, and in both lower limbs and one upper limb in 6 cases. Stenocardia was noted in 22 patients, 9 had had a myocardial infarct, and 11 had a gastric ulcer as well as endarteritis obliterans. Pronounced trophic changes (ulcers) were present in 30 cases. Skin temperature was recorded and capillaroscopy performed in all cases. The author gave stilboestrol or folliculin 10,000 u. intramuscularly daily for about 30 days; in mild cases the injections were given on alternate days. Male cases received testosterone propionate, 10 mg. twice weekly. Women who still menstruated were given stilboestrol 3 or 4 days after their period and continued for 12 to 14 days. If necessary this was repeated 2 or 3 times. Patients reported a feeling of warmth in their limbs 30 to 40 minutes after the injection, and an alleviation of pain. When inflammatory changes were present 300,000 to 600,000 units of penicillin were given daily.

After the first course of treatment was finished the skin temperature of the affected limbs was raised 2° C. compared with the first reading; in 80% of the cases the pain ceased and the ulcers had cleared. Only a minimal effect was noticed in 11%, 4% showed no change, and 5% had to have an amputation of one or more limbs. Contact was maintained with 42 patients for from 6 to 24 months: 24 continued to do well, 7 had a relapse but did well after a second course of treatment, the others relapsed very soon after treatment.

The author suggests that sex hormones (folliculin and stilboestrol) help to produce a good collateral blood supply in all cases of arterial insufficiency irrespective of aetiology. *N. Chatelain*

221. **Fluorescein Test of Circulation Time in Peripheral Vascular Disease**
A. G. MACGREGOR and E. J. WAYNE. *British Heart Journal* [*Brit. Heart J.*] **13**, 80–88, Jan., 1951. 13 refs.

The fluorescein test, as introduced in 1942 by Lange and Boyd (*Med. Clin. N. Amer.*, **26**, 943) and modified by Nathanson and Merliss (*Proc. Soc. exp. Biol., N.Y.*, 1943, **53**, 261), when performed under standardized conditions, was found to be a useful help in the objective evaluation of the severity of peripheral occlusive arterial disease and also as an index of the response to treatment. Although of great value, it cannot replace such other tests as plethysmography and reactive hyperaemia.

In 15 normal subjects, the average " arm-time " (right to left arm) was 16·6 seconds, and the average " foot-time " (right arm to dorsa of feet), 27 seconds. Prolongation of both readings was found in myxoedema, heart failure, and thyrotoxicosis. The difference between foot- and arm-times reflects mainly the degree of occlusive arterial disease present, and figures in excess of 13 seconds were usually found to be of significance. In 5 out of 30 patients arterial disease existed when the fluorescein test was normal. In patients treated by unilateral sympathectomy an average acceleration of 17 seconds relative to the untreated leg occurred in the circulation times to the feet. *A. I. Suchett-Kaye*

Disorders of the Blood

222. **Prevention of Toxicity of Massive Doses of A-methopterin by Citrovorum Factor**
J. H. BURCHENAL and G. M. BABCOCK. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **76**, 382–384, Feb., 1951. 11 refs.

223. **Role of Aureomycin and Citrovorum Factor in "Folic Acid" Deficiencies**
H. A. WAISMAN, M. GREEN, J. C. MUNOZ, A. RAMENCHIK, and J. B. RICHMOND. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol. N.Y.*] **76**, 384–388, Feb., 1951. 4 figs., 3 refs.

224. **Trial of β-Naphthyl-di-2-chloroethylamine in Leukaemia, Hodgkin's Disease, and Allied Disorders**
C. GARDIKAS and J. F. WILKINSON. *Lancet* [*Lancet*] **1**, 137–139, Jan. 20, 1951. 8 refs.

The results are reported of a trial of β-naphthyl-di-2-chloroethylamine ("R 48") by mouth in 25 patients with leukaemia, Hodgkin's disease, and allied disorders. Of 8 patients with chronic lymphatic leukaemia 2 responded to the treatment satisfactorily, in 2 the results were disappointing, and 3 died soon after the first course; the eighth patient is still being treated. Of 4 cases of myeloid leukaemia, 2 responded well and one not at all; one patient died soon after the first course was completed and one is still under early treatment; 2 patients with Hodgkin's disease died, one did not respond at all, and 4 did well. A case of mycosis fungoides responded well, but cases of giant follicular reticulosis and lymphosarcoma did not. Gross haematuria, a generalized purpuric rash without thrombocytopenia, and a transient maculo-papular rash were noted as complicating symptoms unrelated to the size of the dose but relieved by stopping treatment. The authors consider the results less favourable than those obtained when the β-chloroalkylamines are given intravenously. If for any reason intravenous therapy is contraindicated R 48 may be considered as a possible therapeutic agent.
Janet Vaughan

225. **Lesions of the Fundus Oculi in Acute Leukaemia.** (Les lésions du fond de l'œil dans la leucose aiguë)
M. A. DOLLFUS and N. D. CAT. *Sang* [*Sang*] **22**, 1–11, 1951. 1 fig., 14 refs.

The fundus oculi was examined in 27 cases of acute leukaemia. The three important changes are: oedema of the retina and papilla with venous engorgement; leukaemic exudates; and haemorrhages. Some of these last are fusiform with a white centre, presenting the shape of a canoe. These are regarded as pathognomonic.
A. Piney

226. **Infectious Origin of Acute Leukemia**
E. E. BROWN. *Archives of Pediatrics* [*Arch. Pediat.*] **68**, 110–119, March, 1951. 2 figs., bibliography.

ANAEMIA

227. **The Hypoplastic Iron Deficiency Anaemias.** (Les anémies ferriprives hypoplastiques)
P. CROIZAT, L. REVOL, R. CREYSSEL, P. BOSSON, and P. MOORE. *Sang* [*Sang*] **22**, 98–108, 1951. 1 fig.

Observations are reported on the little-known iron deficiency anaemias associated with hypoplasia of the marrow. Treatment with large doses of iron is successful and the authors suggest that iron serves not only for the production of haemoglobin, but also for the synthesis of various cellular enzymes essential in erythropoiesis.
A. Piney

228. **Changes in Structure of the Blood Platelets in Certain Diseases of the Blood.** (Изменения структуры кровяных пластинок при некоторых заболеваниях системы крови)
T. V. KENIGSON. Терапевтический Архив [*Terap. Arkh.*] **22**, No. 6, 48–56, 1950. 7 refs.

A study of the morphology of the blood platelets has shown that they may be classified according to their age and that "irritation" forms and degenerate forms can be recognized. Basing his classification on that of Jurgens and Graupner (*Folia haemat., Lpz.*, 1937, **57**, 263) the author investigated the formula of distribution of these forms in haemolytic jaundice (before and after splenectomy) and in pernicious anaemia. The normal distribution is: young forms, 0 to 3·5%; mature forms, 91 to 98%; old forms, 0 to 3%; "irritation" forms, 0 to 4·5%; degenerate forms, *nil*.

In haemolytic jaundice before splenectomy the young and the degenerate forms are increased at the expense of the mature and old forms. After splenectomy there is at first a great increase in young and "irritation" forms, with a rapid fall in the percentage of degenerate platelets, but later old forms increase in number up to 24% of the total. In some cases the percentage of degenerate forms tends to rise again, especially in cases of long standing; this raises the question whether splenectomy is effective in such cases. In pernicious anaemia there is a great increase in old forms during periods of exacerbation; the appearance of young forms in large numbers is the first sign of a remission. Under liver therapy the differential count of platelets gradually returns to normal.
L. Firman-Edwards

229 (*a*). **The Vitamin B_{12} Group of Factors**
E. LESTER SMITH. *British Medical Journal* [*Brit. med. J.*] **1**, 151–152, Jan. 27, 1951. 1 fig., 29 refs.

This is a short review of recent progress in the vitamin-B_{12} field. Vitamin B_{12a} appears to be identical with vitamin B_{12b}, and to be a reduction product of vitamin B_{12}. The presence of a cyanide group has been established in the vitamin-B_{12} molecule, coordinated with the cobalt atom. Vitamin B_{12b} lacks this cyanide group. Two new factors, vitamin B_{12c} and vitamin B_{12d},

have been isolated from *Streptomyces griseus* fermentation liquors. Vitamin B_{12c} can be distinguished from the other factors by its characteristic absorption spectrum. Vitamin B_{12d} and vitamin B_{12b} have identical absorption spectra, but they can be separated chromatographically. The behaviour of vitamin B_{12c} and B_{12d} on microbiological culture plates differs from that of vitamins B_{11} and B_{12b}. With regard to its biological significance there now seems little doubt that vitamin B_{12} is Castle's "extrinsic factor". It has also recently been shown to have a number of other biological activities which are briefly referred to in this article. *L. J. Davis*

229 (*b*). **Effect of Vitamin B_{12} in Pernicious Anaemia and Subacute Combined Degeneration of the Cord**
C. C. UNGLEY. *British Medical Journal* [*Brit. med. J.*] **1**, 152–157, Jan. 27, 1951. 5 figs., 4 refs.

Since commercial preparations of vitamin B_{12} derived from microbic fermentation liquors may consist of varying proportions of the several members of the group, it is obviously desirable to determine the comparative therapeutic efficacy of these different factors. The present paper presents the results of therapeutic trials with vitamin B_{12c} in crystalline form. Doses were graded logarithmically—10, 20, 40, 80, and 160 μg.—and 28 responses were observed in 24 patients, the methods being similar to those previously used by the same author when studying the action of vitamin B_{12}. Although the haematological responses showed the usual individual variations, the mean of the 28 responses was almost identical with the response expected from equal doses of vitamin B_{12}. Twenty patients with little or no neurological involvement have subsequently been maintained for 4 to 9 months on doses of 10 μg. every 2 weeks. None of these patients has shown any symptoms of relapse, and the results are as good as those observed with similar maintenance doses of vitamin B_{12}. Vitamin B_{12c} was also given to 6 patients with subacute combined degeneration of the cord, and to 8 patients with minor neurological manifestations. None of the patients became worse and all except 2 were improved. It is concluded that, subject to the limitations of the experiment, vitamins B_{12} and B_{12c} are equally effective in all respects in the treatment of pernicious anaemia.
L. J. Davis

230. **Haemopoietic Activity of Vitamins B_{12c} and B_{12d} in Pernicious Anaemia**
J. N. MARSHALL CHALMERS. *British Medical Journal* [*Brit. med. J.*] **1**, 161–164, Jan. 27, 1951. 1 fig., 14 refs.

This paper records the primary haematological response in pernicious anaemia to crystalline vitamin B_{12c} (9 cases) and vitamin B_{12d} (5 cases). In each case a single dose of 20 μg. was injected intramuscularly. The gain in the erythrocyte count in 15 days was taken as the measure of haematological improvement. The responses were reasonably satisfactory in all cases when compared with the expected figures, calculated by Della Vida and Dyke's formula. There was also marked clinical improvement within the period of observation.
L. J. Davis

231. **Two Cases of Pernicious Anaemia Treated with Vitamin B_{12d}**
G. C. K. REID. *British Medical Journal* [*Brit. med. J.*] **1**, 164–165, Jan. 27, 1951. 2 figs.

Two cases of pernicious anaemia have been successfully treated with vitamin B_{12d} in the very small dosage of 10 μg. Both showed the anti-anaemic activity to be of the same order as that of crystalline vitamin B_{12}.

In one case 10 μg. of vitamin B_{12d} gave the same response as 1 ml. of "examen", having full anti-anaemic activity at that dose level.—[Author's summary.]

232. **A Positive Coombs Reaction in Pernicious Anaemia**
J. G. SELWYN and S. S. ALEXANDER. *British Medical Journal* [*Brit. med. J.*] **1**, 564–565, March 17, 1951. 13 refs.

233. **Treatment of Pernicious Anemia with Citrovorum Factor**
L. M. MEYER, C. M. BRAHIN, and A. SAWITSKY. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **76**, 86–90, Jan., 1951. 5 figs., 4 refs.

Sauberlich and Bauman (*J. Biol. Chem.*, 1948, **176**, 165) first described the citrovorum factor (C.F.), present in liver; it is necessary for the growth of *Leuconostoc citrovorum*. This paper describes the results of the parenteral administration of C.F. to 5 patients with pernicious anaemia in relapse. The C.F. was given in the form of a concentrate containing 20,000,000 C.F. units per ml. (One C.F. unit is equivalent to 0·000015 μg. of the anhydrous free acid of C.F.) Four patients received 1 ml. of this concentrate intramuscularly daily, and the fifth received half this dose. This was followed by a submaximal reticulocyte response and a suboptimal rise in the levels of haemoglobin and erythrocytes. There was a moderate improvement in appetite and general well-being, but this was not so dramatic as that obtained with adequate therapy with liver extract, vitamin B_{12}, or folic acid. In one case distinct neurological improvement occurred. Although the daily administration of 40,000,000 units produced a further rise in erythrocyte count in 3 cases, normal blood values were not attained.
A. W. H. Foxell

234. **The Response of Megaloblastic Macrocytic Anaemia to Crystalline Penicillin G. Preliminary Report**
H. FOY, A. KONDI, and A. HARGREAVES. *British Medical Journal* [*Brit. med. J.*] **1**, 380–383, Feb. 24, 1951. 4 figs., 6 refs.

This single case record deals with a Kikuyu woman who had a relapsing macrocytic anaemia considered to be of nutritional origin. On her first admission to hospital she was in her third relapse. She had typical megaloblastic marrow, and free hydrochloric acid was present, although reduced, in the gastric juice. She was treated with "marmite"; when the reticulocyte response had begun she developed pulmonary congestion and was given 400,000 units of benzyl penicillin daily for 7 days.

Reticulocytes rose to a maximum of 37%, erythrocyte count rose from 1,340,000 to 3,440,000 per c.mm., but haemoglobin rose only from 4·0 to 7·7 g. per 100 ml.; this sort of response is common in Kenya. Detection and treatment of *Entamoeba histolytica* infestation brought about a further improvement. Eleven months later she was admitted in a fourth relapse. This time she had histamine-fast achlorhydria; no intestinal parasites were found. There were no signs of neurological disease. After 4 days, the reticulocyte count remaining low, she was given benzyl penicillin 400,000 units daily, and no other treatment. Reticulocytes rose to 36% on the 5th day, and on the 6th all megaloblasts had disappeared from the marrow. In 14 days the erythrocyte count rose from 1,760,000 to 3,250,000 per c.mm. and haemoglobin from 5·0 to 8·7 g. per 100 ml.

The authors suggest that the penicillin may have acted either by destroying some organism that was competing for haematopoietic substances like folic acid or vitamin B_{12}, by removal of some haematopoietic antagonist, by preventing the absorption of glutamic acid by competing organisms, which might thus interfere with the synthesis of folic acid, or by affecting the metabolism and excretion of some essential amino-acid. These points have now to be tested and the results confirmed.

M. C. G. Israëls

235. **The Response of Patients with Pernicious Anemia, with Nutritional Macrocytic Anemia and with Tropical Sprue to Folinic Acid or Citrovorum Factor**

T. D. Spies, G. G. Lopez, F. Milanes, R. L. Toca, A. Reboredo, and R. E. Stone. *Southern Medical Journal* [*Sth. med. J. Bgham, Ala*] **43**, 1076–1082, Dec., 1950. 4 figs., 17 refs.

Citrovorum factor and folinic acid are closely related, if not identical, substances having close structural and functional affinities with folic acid. Citrovorum factor is so named because it was originally discovered as a growth factor for *Leuconostoc citrovorum*. Folinic acid was encountered in an investigation of substances capable of inhibiting the action of folic acid antagonists, and was found to be much more effective than folic acid in this respect. These substances occur in nature and have also been synthesized. Crude folinic acid was shown by May *et al.* to be highly effective in the treatment of nutritional megaloblastic anaemia of monkeys, and now a report is given of clinical trials with these substances in human cases of megaloblastic anaemia.

A study was made of 10 patients with megaloblastic macrocytic anaemia in relapse: 4 of them had pernicious anaemia, 4 tropical sprue, and 2 nutritional anaemia. Folinic acid, 200 units daily for 10 days, was given by intramuscular injection to 6 patients. "One unit is approximately 1 μg. of pure citrovorum factor and equivalent to 10 Lederle units or 4,900 Baumann–Sauberlich units." Two patients, with pernicious anaemia and tropical sprue respectively, showed submaximal clinical and haematopoietic responses, but the other 4 patients [types of anaemia not specified] did not respond at all. The remaining 4 patients, including one case of pernicious anaemia and one of tropical sprue [no details given of the other 2], received intramuscular injections of citrovorum factor for 10 days, the daily dose being 20,000,000 units. "One unit is equivalent to 0·001 μg. of pteroylglutamic acid (folic acid), in other words, 10,000,000 units equal 1 mg. of pteroylglutamic acid." In all cases in this group clinical and haematopoietic responses were considered to be maximal.

L. J. Davis

236. **Pernicious Anaemia Developing Four Years after Total Gastrectomy.** (Anémie de Biermer 4 ans après une gastrectomie totale)

J. Bousser and P. Blondet. *Sang* [*Sang*] **22**, 140–143, 1951. 16 refs.

A case of pernicious anaemia developing 4 years after total gastrectomy is described; the rarity of the condition as determined from the literature is briefly discussed.

A. Piney

237. **Vitamin B_{12} and Folic Acid in Megaloblastic Anaemia after Total Gastrectomy**

N. S. Conway and H. Conway. *British Medical Journal* [*Brit. med. J.*] **1**, 158–161, Jan. 27, 1951. 34 refs.

The case is reported of a man aged 47 on whom a total gastrectomy was performed because of extensive scarring resulting from swallowing corrosive fluid. Two years later a mild macrocytic anaemia was noted. When he was seen after the lapse of nearly 2 more years, close on 4 years after his gastrectomy, he was seriously ill with a severe macrocytic anaemia, the erythrocyte count being 950,000 per c.mm., the blood film typical of pernicious anaemia, and the sternal marrow megaloblastic. No neurological manifestations were present. Treatment was instituted with injections of vitamin B_{12} and was followed by a reasonably good, but slightly suboptimal, haematological response, and by marked clinical improvement. After 5 weeks, however, there was no further rise in the erythrocyte count above a level of 3,800,000 per c.mm. during the next 6 weeks. A sternal-puncture smear at this time was considered to show a normal marrow picture. Injections of vitamin B_{12} were now supplemented by a daily dose of 20 mg. of folic acid [? orally], and the erythrocyte count rose to 4,600,000 per c.mm. within 2 weeks. The relationship of the anaemia to other megaloblastic anaemias as regards treatment with vitamin B_{12} and folic acid is discussed.

L. J. Davis

238. **Clinical Trials of A.C.T.H. in Haemolytic Anemia**

L. S. P. Davidson, J. J. R. Duthie, R. H. Girdwood, and R. J. G. Sinclair. *British Medical Journal* [*Brit. med. J.*] **1**, 657–660, March 31, 1951. 1 fig., 4 refs.

The authors have treated 3 cases of haemolytic anaemia with ACTH in a dose of 100 mg. daily for 10 days. ACTH rapidly controlled the haemolytic phenomena in one case of acquired haemolytic anaemia; the symptoms have not recurred, and the Coombs test was negative and an abnormal antibody no longer present 8 months after treatment was started, although both remained positive for some time after symptoms had

completely ceased. In 2 cases of congenital haemolytic anaemia there was little or no response to the administration of ACTH in similar doses. The authors suggest that the control of haemolysis by ACTH in acquired haemolytic anaemia is not due to suppression of the production of abnormal antibodies. *Janet Vaughan*

239. **Spherocytosis and Increased Fragility Occurring in Erythroblastosis Fetalis associated with ABO Incompatibility**
G. C. ROBINSON, R. M. PHILLIPS, and M. PRYSTOWSKY. *Pediatrics* [*Pediatrics*] **7**, 164–171, Feb., 1951. 14 refs.

Four cases of hemolytic disease of the newborn infant are reported. There was ABO incompatibility and high maternal immune antibody titre after delivery. Immune antibody was demonstrated in the sera of 3 of the 4 infants. The difficulties in making an unequivocal diagnosis are discussed and the diagnostic value of immune antibody in the infant's serum is emphasized. The presence of spherocytosis and altered erythrocyte hypotonic fragility during the hemolytic phase is noted. These findings are similar to cases of acute hemolytic anaemia in adults previously reported.—[Authors' summary.]

240. **Erythroblastosis Fetalis. VII. Treatment with Exchange Transfusion**
L. K. DIAMOND, F. H. ALLEN, and W. O. THOMAS. *New England Journal of Medicine* [*New Engl. J. Med.*] **244**, 39–49, Jan. 11, 1951. 10 figs., 13 refs.

The bulk of this paper is devoted to a detailed and exact description of the equipment used and the technique adopted for exchange transfusion, by the umbilical vein, in infants suffering from haemolytic disease of the newborn (erythroblastosis foetalis). Only female donors are used and care must be exercised to exclude women whose serum contains significant amounts of Rh antibody. The routine use of group-O donors is recommended, and the donor blood should be Rh-negative in cases in which the mother of the affected infant is Rh-negative, If the mother is Rh-positive, blood that is not agglutinated by her serum should be used. Bank blood has been found to be satisfactory for exchange transfusion after storage for as long as about 2 weeks. Whenever time permits it is advisable to cross-match baby and donor, but in an emergency group-O Rh-negative bank blood to which A and B substances have been added should be used. The transfusion is terminated by giving very slowly 2 ml. of a 10% solution of calcium gluconate mixed with 2 ml. of vitamin-K solution. Subsequently, penicillin and sulphadiazine are always given for 2 or 3 days. Oxygen is also administered in high concentration, and crude liver extract intramuscularly for 5 days.

The authors have been impressed with the rapidity with which the jaundice fades after exchange transfusion, none usually being detectable after 4 days. The blood count is repeated when the baby is 4 to 5 days old and a small transfusion given as indicated. Almost all the babies are discharged from hospital between the fifth and twelfth day.

Although it is appreciated that not all Rh-positive babies of sensitized Rh-negative mothers are in need of exchange transfusion, four indications are given for its immediate performance: (1) if the baby, within 24 hours, has clinically apparent erythroblastosis foetalis; (2) if the baby is Rh-positive and the mother's titre of Rh antibody was 1 : 16 or higher at any time during pregnancy; (3) if the baby is Rh-positive and there is an unfavourable past history; and (4) if the Rh-positive baby is immature. In those cases where the likelihood of kernicterus seems high, particularly in the immature male infant of a highly sensitized mother, a second exchange transfusion has been given 12 to 24 hours after the first one. This also applies to babies who develop intense jaundice within 24 hours of an exchange transfusion performed at birth.

Details are given of 391 exchange transfusions, including the amount of blood removed, the ages of the babies at the start of the procedure, and the outcome in babies with erythroblastosis foetalis due to anti-D antibody.

[The procedures employed cannot be briefly described, and those interested are advised to refer to the original paper.] *Jas. M. Smellie*

HAEMORRHAGIC DISEASES

241. **Primary Thrombocytopenic Purpura and Acquired Hemolytic Anaemia. Evidence for a Common Etiology**
R. S. EVANS, K. TAKAHASHI, R. T. DUANE, R. PAYNE, and CHI-KONG LIU. *Archives of Internal Medicine* [*Arch. intern. Med.*] **87**, 48–65, Jan., 1951. 1 fig., 28 refs.

It is argued that essential (primary) thrombocytopenic purpura is due to an immunity mechanism similar to that in acquired idiopathic haemolytic anaemia, and that a spectrum-like relationship exists between the two diseases. This contention is based mainly upon the following observations. Analysis of a group of 18 patients with acquired haemolytic anaemia shows that in 10 of them the platelet counts were normal or only slightly depressed, in 4 of them there was thrombocytopenia but no purpura, while in the remaining 4 there was thrombocytopenia with purpura. Of 11 patients with thrombocytopenic purpura without anaemia, the erythrocytes of 6 were agglutinated by anti-globulin serum, while in the remaining 5 no such reactions occurred. Experiments *in vitro* showed that a thrombocyte-agglutinating factor is present in the serum of patients with primary thrombocytopenic purpura. The authors sound a note of caution in interpreting the significance of these experiments. *L. J. Davis*

242. **The Female Carrier of Haemophilia. A Clinical and Laboratory Study**
C. MERSKEY and R. G. MACFARLANE. *Lancet* [*Lancet*] **1**, 487–490, March 3, 1951. 4 figs., 9 refs.

Known and suspected carriers of haemophilia were compared with normal female controls in respect of: (1) the history of abnormal bleeding; (2) the coagulation

time as estimated by Bürker's and Lee and White's methods: (3) the prothrombin consumption on clotting; and (4) the titration of anti-haemophilic factor in whole blood. It was found that 5% of normals, 47% of known carriers, and 17% of mothers of one haemophilic son bled excessively after tooth extraction (out of 100 normal persons and 19 known and 12 suspected carriers). The coagulation times and antihaemophilic-factor content of the blood showed no differences between the groups. Of 21 known carriers 3 showed abnormal prothrombin consumption on clotting; these 3 bled excessively after tooth extraction. The results were too inconstant to be of diagnostic value. *G. Discombe*

243. **The Differential Diagnosis of Haemophilia on Biological Grounds.** (Diagnostic biologique différentiel des hémophilies)
M. GUILLOT and A. FIEHRER. *Sang* [*Sang*] **22**, 114–122, 1951. 5 figs.

The authors briefly discuss true haemophilia and its differential diagnosis. A valuable table for the distinction of true haemophilia, para-haemophilia, and the pseudo-haemophilia of Castex and Pavlovsky is presented. *A. Piney*

244. **Haemophilic Arthropathy. Beneficial Results of Irrigation with Thrombin Solutions.** (Arthropathies hémophiliques. Heureux effets du lavage par les solutions de thrombine)
G. GIRAUD, H. LATOUR, and A. LÉVY. *Sang* [*Sang*] **22**, 132–136, 1951. 13 refs.

245. **Hemorrhagic Diathesis with Ascorbic Acid Deficiency during Administration of Anterior Pituitary Corticotropic Hormone (ACTH)**
M. STEFANINI and M. C. ROSENTHAL. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 806–808, Dec., 1950. 12 refs.

Two patients developed haemorrhagic manifestations, presumably due to ascorbic acid deficiency, while receiving high doses of adrenocorticotrophic hormone (ACTH). One received 2·7 g. ACTH, which was twice as potent as a certain standard " LA–1–A ", in 125 days. The other patient received 28 mg. of an ACTH preparation, 25 to 30 times as potent as LA-1-A, in 9 days. Petechiae appeared in the first patient on the 115th day and in the second on the 9th day. In both, large petechiae were produced on pricking the skin. On the administration of ascorbic acid no further haemorrhagic manifestations occurred.

The diagnosis was based on: (1) haemorrhagic manifestations with only moderate disturbance of other factors of haemostasis, especially following minimal trauma to the skin; (2) low plasma ascorbic acid level (0·17 and 0·4 mg. per 100 ml.) and low urinary excretion of ascorbic acid; (3) low plasma ascorbic acid tolerance curve (in the one case where this was performed) after intravenous injection of 1 g.; (4) therapeutic effect of ascorbic acid on skin haemorrhages.

It is pointed out that ascorbic acid deficiency is probably not common in the course of ACTH therapy, but should be considered if haemorrhagic signs appear during prolonged administration of this hormone. *Norval Taylor*

246. **Vitamin K in the Prevention of Haemorrhagic Disease of the Newborn**
J. D. HAY, F. P. HUDSON, and T. S. RODGERS. *Lancet* [*Lancet*] **1**, 423–425, Feb. 24, 1951. 14 refs.

The hypoprothrombinaemia occurring normally in the first few days of life may be prevented by the administration of vitamin K. The present paper records an investigation, carried out at the five largest maternity units in Liverpool, of the effect of routine administration of vitamin-K analogue to mothers during labour. The 4,602 children of treated mothers were compared with 12,136 children whose mothers had received no vitamin K. Haemorrhagic disease of the newborn occurred in 11 of the test infants (1 in 418 cases) and in 23 of the controls (1 in 527 cases).

It is concluded that vitamin K does not always succeed in preventing haemorrhagic disease of the newborn and that its routine use in maternity units is not justified except possibly in cases where there is an increased risk of neonatal bleeding. *J. A. Chalmers*

HAEMATOPOIETIC SYSTEM

247. **Hematologic Effects of Regional Nitrogen Mustard Therapy**
J. C. BATEMAN, C. T. KLOPP, and J. K. CROMER. *Blood* [*Blood*] **6**, 26–38, Jan., 1951. 16 refs.

Nitrogen mustard was given by intra-arterial injection to 21 patients with advanced malignant disease with the object of reducing the toxic effect of the drug on the bone marrow and thus enabling larger doses to be given. Total doses of up to 3·1 mg. per kg. were given to these patients. In some cases the venous return from the treated area was obstructed by a ligature, and this was thought to protect the marrow to some extent. The haematological findings are reported in detail. The changes were qualitatively similar to those described after intravenous injection of nitrogen mustard, but larger doses were tolerated and only one patient developed severe bone-marrow hypoplasia. When regional nitrogen-mustard therapy was given to the pelvis the iliac marrow was judged to be more severely depressed than the sternal marrow. *P. C. Reynell*

248. **Cryoglobulinaemia in Multiple Myelomatosis**
A. N. BLADES *British Medical Journal* [*Brit. med. J.*] **1**, 169–171, Jan. 27, 1951. 20 refs.

References have been traced to about a dozen cases in the literature showing cryoglobulinaemia, a term which implies the presence in the plasma of a globulin which precipitates or solidifies on cooling to about 30° C. The phenomenon is reversible on warming to 37° C. and the changes may be repeated indefinitely. Such globulins occur in multiple myelomatosis and have also been found in endocarditis lenta, kala-azar, nephrosis, and in infective arthritis. In the case reported here

the diagnosis of multiple myelomatosis was suggested by the finding of cryoglobulinaemia. The author reviews the hitherto published observations on the serum containing this abnormal globulin, and also discusses the nature of this abnormal protein occurring in multiple myelomatosis. *S. Karani*

249. **Effect of ACTH and Suprarenal Extract on the Bone Marrow**
J. M. YOFFEY, W. K. METCALF, G. HERDAN, and V. NAIRN. *British Medical Journal* [*Brit. med. J.*] **1**, 660–665, March 31, 1951. 43 refs.

The authors have studied the effect of ACTH and adrenal cortical extract on the bone marrow of guinea-pigs. A quantitative technique to determine the number of nucleated cells in the marrow is described. This was applied to 25 normal guinea-pigs, to 9 guinea-pigs which had received 0·1 ml. of " eschatin " per 100 g. body weight intraperitoneally, and to 10 guinea-pigs which had received 1 mg. of ACTH per 100 g. intraperitoneally. The normal guinea-pig marrow contained an average of 1,236,000 nucleated cells per c.mm., of which 144,800 were lymphocytes. There was no demonstrable increase of damaged cells in the marrow 6 hours after giving either ACTH or the adrenal extract, but there was a statistically significant increase in the lymphocyte content after giving the latter, and an increase almost reaching the significant level in the case of ACTH. It is suggested that increased uptake of lymphocytes from the blood by the bone marrow may possibly be a contributory factor in the lymphopenia which may follow the administration of ACTH or steroid hormones.

Janet Vaughan

250. **The Bone Marrow in Secondary Polycythemia associated with Cor Pulmonale**
K. BRAUN. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **21**, 149–152, Feb., 1951. 1 fig., 10 refs.

The bone marrow was studied in 16 patients with secondary polycythemia associated with chronic cor pulmonale. A relative hyperplasia of the nucleated red cells was consistently found. The number of myeloid cells and the number of megakaryocytes were not increased. These findings differ from those of polycythemia vera and indicate that the mechanism of erythropoiesis in polycythemia secondary to anoxemia differs from that in polycythemia vera.—[Author's summary.]

251. **The Iron in Bone-marrow Biopsy Material.** (Das Eisen im punktierten Knochenmark)
W. MASSHOFF and P. GRUNER. *Acta Haematologica* [*Acta haemat., Basel*] **5**, 19–29, Jan., 1951. 26 refs.

In order to find out whether the amount of iron in the bone marrow which can be demonstrated histochemically can be of value for diagnosis or therapy, alcohol-fixed material from bone-marrow biopsies in 177 cases of various disorders was stained with Prussian blue. Iron was absent in 105 cases, and the others were graded as having mainly diffuse iron, or moderate or large amounts of granular iron. This storage iron is found only in the cytoplasm of reticular cells, but a relationship could not be proved either between the amount of iron and marrow cellularity or between the iron and the underlying disease, the degree of anaemia present, the previous administration of iron, or previous blood transfusions. In only half the cases treated with iron or transfusions was it possible to demonstrate iron in the bone marrow. The authors conclude that the storage iron in the marrow which is mainly granular does not play a very appreciable part in blood formation, but it is possible that histochemical methods are not suitable for assessing iron metabolism. It is not clear why and how the marrow stores iron. The authors believe that they have conclusively refuted the theories put forward by the team of workers at the Peter Bent Brigham Hospital, Boston, led by Rath and Finch, who, in one of their most recent papers (*Blood*, 1950, **5**, 983), maintain that storage iron is available for haemoglobin synthesis when necessary. It is only haemosiderin which can be seen as fine granules in sections, but ferritin is not demonstrable histochemically. *E. Neumark*

252. **A Study of the Erythroblasts in Cooley's Anaemia.** (Untersuchungen über die Biologie des Erythroblasten in der Thalassaemia major)
G. ASTALDI, P. TOLENTINO, and C. SACCHETTI. *Helvetica Paediatrica Acta* [*Helv. paediat. Acta*] **6**, 50–61, Feb., 1951. 5 figs., 40 refs.

Bone-marrow biopsy material from 8 children with Cooley's anaemia was studied by tissue culture in order to elucidate the nature of the erythroblastic hyperplasia. Cell differentiation was followed by placing material in a fluid medium of heparinized plasma and Tyrode's solution. The early cells soon diminished in number and disappeared in 18 to 24 hours; nucleated red cells as well as reticulocytes matured gradually in 48 hours. Cell proliferation was observed in marrow fragments planted in solid media consisting of heparinized plasma with protamine, Tyrode's solution, and colchicine, the last substance inhibiting the early phases of mitosis. This caused a steady increase of cells, and the increasing number of mitoses was used in assessing the degree of proliferation by means of the " stathmo-kinetic index ", which was established separately for basophilic and polychromatic erythroblasts. The proliferative activity of basophilic erythroblasts in media containing plasma from the same patient was much higher than normal, but polychromatic forms behaved to all intents and purposes normally; orthochromatic cells showed no mitotic activity. In Cooley's anaemia basophilic erythroblasts took up to 60 hours to differentiate into polychromatic forms. Maturation was therefore much slower than normal and the loss of nuclei was also slower. Delay in differentiation was most marked in the severe cases and was regarded as a sign of marrow exhaustion. When marrow fragments were placed in media made up with plasma from healthy persons, the observations were similar. Marrow from normal persons, suspended in media made up with plasma from cases of Cooley's anaemia, showed no delay in differentiation or increased proliferative activity of erythroblasts. *E. Neumark*

Respiratory Disorders

253. **Administration of Penicillin in the Treatment of Empyema.** (Применение пенициллина в лечении гнойных плевритов)
V. N. SARDYKO. Клиническая Медицина [*Klin. Med., Mosk.*] No. 1, 56–61, 1951. 1 fig., 14 refs.

After tracing the development of the treatment of empyema during the last 100 years, the author describes his own technique, consisting in repeated aspiration of the pleural contents and the intrapleural injection of 50,000 to 200,000 units of penicillin. In the present investigation 23 persons were studied; the nature of the pleural contents was studied bacteriologically and cytologically, the penicillin sensitivity of the organism tested, and the concentration of penicillin in blood and pleural fluid estimated. Although penicillin was also given intramuscularly as a precaution against general infection, in no case was penicillin found in the pleural fluid, even after 24 hours, until introduced directly into the cavity. It may therefore be assumed that penicillin in the blood stream does not pass the pleural barrier. Penicillin introduced intrapleurally remains at a therapeutic level in the fluid for 2 days in acute cases, and from 5 to 7 days in chronic cases. That the difference is due to greater permeability of the pleura in acute pleurisy was shown by the finding of a concentration of penicillin in the blood up to 0·248 units per ml. 30 minutes after injection in acute cases, as against 0·093 units per ml. after 1 hour in a chronic case. This titre fell after 4 hours to 0·062 units per ml. in acute cases, and to 0·03 units per ml. in chronic cases. In 4 out of the 5 cases in which this treatment was ineffective the condition was complicated by abscess of the lung, while the empyema was chronic in the fifth.

L. Firman-Edwards

254. **Sulphonamides and Acute Tonsillitis. A Controlled Experiment in a Royal Air Force Community**
T. C. MACDONALD and I. H. WATSON. *British Medical Journal* [*Brit. med. J.*] **1**, 323–326, Feb. 17, 1951. 1 ref.

The authors describe a controlled experiment designed to test a recent statement by Anderson (*Brit. med. J.*, 1949, **2**, 860) that the efficacy of the sulphonamides has never been convincingly demonstrated in the treatment of the acute throat and that their use is not altogether free from danger. The cases were drawn from a Service (R.A.F.) community of about 4,000 men, 82 consecutive cases of acute tonsillitis being divided at random into two equal groups, one receiving a total of 25 g. (50 tablets) of "sulphatriad" (each tablet containing sulphathiazole 0·185 g., sulphadiazine 0·185 g., and sulphamerazine 0·130 g.) and the other an equal number of lactose tablets, identical in appearance, at the same (4-hourly) intervals over the same period (4 days). The clinician in charge of the cases did not know which tablets were being given. Cultures of the nose and throat were taken, but β-haemolytic streptococci were found to be present in only about half the cases in each group. Standardized records were kept of the severity of selected signs and symptoms (of which the authors regard temperature, pain in the throat, and the presence of exudate on the tonsils as the most reliable), and the subjective opinion of the clinician in charge as to clinical progress after about 72 hours' treatment was also recorded in each case. There was only one complication among the 82 cases, and no toxic effects of the drugs were noted.

When the rapidity of recovery was assessed on the basis of the objective records of signs and symptoms, it was found that there was no difference between control and treated cases, nor was there any significant relationship between rapidity of cure and the presence or absence of β-haemolytic streptococci in either group. On the other hand, there was a marked difference between treated and control groups on the basis of the doctor's assessment, there being significantly more cases of "good cure" amongst the former than the latter (34 as compared with 19). It was not felt, however, that the positive subjective findings should overrule the negative results shown by the objective clinical records, and the authors conclude that from a severely practical point of view simpler and potentially less dangerous remedies than sulphonamides must be recommended. They admit that no light was thrown by the experiment on the value of the drugs for the control of complications or in preventing epidemic spread.

J. V. Armstrong

255. **"Sore Throat" in General Practice**
J. B. LANDSMAN, N. R. GRIST, R. BLACK, D. MCFARLANE, W. BLAIR, and T. ANDERSON. *British Medical Journal* [*Brit. med. J.*] **1**, 326–329, Feb. 17, 1951. 1 fig., 2 refs.

The authors studied a series of 95 cases of "sore throat" occurring in general practice in an urban district, noting certain points of epidemiological interest and, in view of recent criticisms, observing the effects of treatment with sulphonamides. Uniform records of the duration of signs and symptoms were kept, and in all cases cultures were taken from the throat and post-nasal space, the cases being thus divided into two groups —those with normal flora, and those with varying numbers of β-haemolytic streptococci on culture. Less than one-half of the cases (46%) were classed as streptococcal in origin, an observation of some interest and importance since it is a common misapprehension that acute tonsillitis is almost always of streptococcal origin.

In the streptococcal cases headache, anorexia, vomiting, sweating, chills, and rigors predominated, whereas in the other group there was a predominance of symptoms more clearly referable to the respiratory tract, such as sneezing, stuffy nose, rhinorrhoea, and cough, and the illness took a rather milder form and tended to be more common in childhood.

An attempt to define the probable bacteriological cause before the result of the throat swabs was known resulted in frequent errors in both groups.

Three different tablets, identical in appearance, were used in treatment, consisting of sulphanilamide (0·5 g.) (26 cases), " sulphatriad " (0·5 g.) (26 cases), and lactose (0·5 g.) (43 cases), and the practitioner in clinical charge did not know which he was using. [No mention is made of dosage.] The main signs and symptoms of which the duration was noted were fever, faucial oedema, and pain. There was little difference, and certainly no statistically significant difference, between the average duration of any of these, whichever tablet was given, there being no indication that either of the sulphonamide tablets was superior to the presumably inert lactose tablet. Complications were few and there was little difference between the effects of treatment in this respect.

The authors conclude that their findings do not support the view that the sulphonamides exert a beneficial effect in the treatment of the acute " sore throat " and that in view of the fact that in about half the cases a streptococcal aetiology was unlikely, the use of drugs which have definite and known dangers is unnecessary, besides being expensive. *J. V. Armstrong*

256. **The Arteriovenous Angiomatosis of the Lung with Hypoxaemia.** [In English]
A. GIAMPALMO. *Acta Medica Scandinavica* [*Acta med. scand.*] Suppl. 248, **139**, 1–67, 1950. 35 figs., bibliography.

A review is given of 57 cases of arteriovenous angiomatosis of the lung. The lesion is due to a developmental dysplasia leading to ectasia of arteries, veins, and capillaries. The symptoms and signs result from the fact that the blood passing through the lesions is unoxygenated, and are proportional to the flow. Although at birth there may be no symptoms, the condition is progressive, the chief manifestations being dyspnoea, cyanosis, polycythaemia, and clubbing of the fingers. There may also be haemorrhage (into the lung or pleura) or air embolism.

Formerly these cases were often misdiagnosed as cases of congenital heart disease, but nowadays a correct diagnosis should be possible. Radiography may show a shadow associated with a murmur, and the dilated vessels entering and leaving may be demonstrable by tomography. The heart is not enlarged. There may be vascular lesions elsewhere, especially telangiectases of the lip.
D. M. Pryce

257. **Mycosis of the Lung due to *Candida albicans*.** (Lungenmykose durch *Candida albicans*)
W. HOFFMEISTER. *Zeitschrift für Klinische Medizin* [*Z. klin. Med.*] **147**, 493–512, 1951. 4 figs., 35 refs.

The radiograph of the chest of a man of 63, who had worked as a seedsman for 34 years and gave no previous history of chest disease, showed increased vascular markings in the lower lung fields. About a year later he developed a left empyema and smears of the pus contained an unidentified branching fungus. The empyema was drained, but the patient's recovery was slow and radiographs showed increasing mottling in both lung fields. After more than 4 months' illness, *Candida albicans* was cultured from the sputum. Treatment with " supronal " and penicillin resulted in clinical and radiological improvement, and *Candida albicans* disappeared from the sputum. Five months later the sputum was again positive, although the patient felt quite well. A bronchogram showed extensive bronchiectasis. Because of the complete absence of symptoms of pulmonary disease in the past the bronchiectasis was considered to have been caused by the mycotic infection.

[*Candida albicans* is very frequently isolated as a commensal in the bronchial flora and commonly appears to be relatively increased when the flora is disturbed by bacterial infection or treatment by antibiotics. In the case described there is no conclusive evidence that the fungus was acting other than as a saprophyte. Indeed, there is considerable doubt whether pulmonary moniliasis exists as a pathological entity.] *J. R. Bignall*

258. **Pulmonary Changes in Uremia**
H. E. BASS and E. SINGER. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 819–823, Nov. 4, 1950. 5 figs., 9 refs.

The subject of the pulmonary changes in uraemia is reviewed. [No new conclusions are reached but there are some good photomicrographs of the condition.] The pulmonary exudate is chiefly the result of left ventricular failure, but the exudate is fibrinous and there is hyperaemia of the alveolar septa; in some cases the fibrin becomes hyalinized. It is suggested that the periphery of the lung escapes these changes to some extent because there is more movement here and thus less stasis. *G. S. Crockett*

PNEUMONIA

259. **Primary Staphylococcal Pneumonia**
M. O. J. GIBSON and J. R. BELCHER. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **20**, 43–55, Jan., 1951. 9 figs., 28 refs.

In this paper the authors are chiefly concerned with primary staphylococcal pneumonia rather than with metastatic infection of the lungs from an extrapulmonary focus. Primary staphylococcal pneumonia most often arises as a complication of epidemic influenza (in the 1918 pandemic some observers noted an incidence of 11% with a high mortality) or in newborn children, while it is the usual cause of death in fibrocystic disease of the pancreas in infants. In the fulminating type the patient, after 3 to 4 days of typical influenza, becomes prostrated and develops a curious cherry-red–indigo-blue cyanosis and a few physical signs in the chest. In the acute but non-fulminating type pleuritic pain frequently develops after 1 or 2 weeks, there is productive cough, and physical signs in the chest become apparent. The authors give brief case histories of 10 such cases, in all of which the patient recovered. The patients were nearly all adults and the incidence of empyema was 40%;

in children it is said to be 50%. Radiologically, multiple cavitation was a common feature and the authors suggest that this is due to distension (the oedematous mucous membrane of a bronchus acting as a one-way valve) rather than to tissue destruction. Bacteriologically, the diagnosis could be confirmed by growth of a pure, or almost pure, culture of the organism (usually *Staphylococcus aureus*) from the sputum, lung puncture, or empyema fluid. The treatment of the disease has been revolutionized by the advent of the sulphonamides and penicillin. In empyema, aspiration and instillation of penicillin is preferred to rib resection and drainage. There is reason to believe that the newer antibiotics will yield even better results. *D. Preiskel*

260. **Clinical Variations in Primary Atypical Pneumonia**
W. S. JORDAN, R. W. ALBRIGHT, F. H. MCCAIN, and J. H. DINGLE. *American Journal of Medicine* [*Amer. J. Med.*] **10**, 3–20, Jan., 1951. 7 figs., bibliography.

This paper records a study of 67 cases of primary atypical pneumonia. The criteria for diagnosis were: (1) radiographic evidence of pulmonary infiltration; (2) no evident bacterial cause; (3) no response to penicillin or sulphonamides; and (4) a compatible clinical course. In half the cases there were discrepancies between physical signs and radiological findings; these were especially marked in the presence of rheumatic or arteriosclerotic heart disease and of emphysema. About 15% resolved by crisis: 25% showed radiological changes in the absence of physical signs, and 18% showed the reverse. The leucocyte count varied greatly and was not helpful in distinguishing between primary atypical and bacterial pneumonia. In 60% of cases a rise in the cold haemagglutinin titres occurred; there was a rise in streptococcal MG agglutinins in rather fewer cases; neither of these could be clearly related to the clinical severity. *Henry Cohen*

261. **Nebulized Cortisone in Bacterial Pneumonia**
W. H. REEDER and G. S. MACKEY. *Diseases of the Chest* [*Dis. Chest*] **18**, 528–534, Dec., 1950. 7 figs., 4 refs.

A patient suffering from pneumococcal pneumonia and sensitive to penicillin was given cortisone by aerosol inhalation; 5 to 8 mg. of cortisone acetate in normal saline was inhaled half-hourly or hourly for 33 hours (total dosage is not stated, but seems to have been about 330 mg.). Administration of the drug resulted in a marked amelioration of symptoms, though no radiological improvement occurred and pneumococci were found on blood culture 12 hours after the start of treatment. When administration of the drug was stopped symptoms reappeared. The patient was subsequently treated with aureomycin and recovered.

Cortisone, therefore, can apparently be absorbed and can produce an effect upon symptoms when given by aerosol inhalation. It does not, however, seem to affect the disease process in the lungs. The inhalations did not produce any irritation of the trachea or bronchi.
John Forbes

262. **The Efficacy of Modified Oral Penicillin Therapy of Pneumococcal Lobar Pneumonia**
R. AUSTRIAN, G. S. MIRICK, D. E. ROGERS, S. M. SESSOMS, P. A. TUMULTY, W. H. VICKERS, and C. G. ZUBROD. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **88**, 264–269, March, 1951. 12 refs.

A series of 43 cases of pneumococcal lobar pneumonia was treated by giving an initial dose of 300,000 units of benzyl penicillin intramuscularly, followed by oral treatment with 300,000 units of benzyl penicillin every 12 hours together with 1 g. of "benemid" (*p*-di-N-propylsulphamylbenzoic acid), a drug which decreases the renal excretion of penicillin. These cases have been compared with 57 similar cases of pneumonia which were treated with 300,000 units of sodium benzyl penicillin intramuscularly every 12 hours. There was no significant difference between the excellent results obtained in both groups. *John Forbes*

263. **The Treatment of Pneumococcal Lobar Pneumonia with Oral Aluminum Penicillin**
J. C. HARVEY and G. S. MIRICK. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **88**, 270–275, March, 1951. 15 refs.

Oral aluminium penicillin tablets containing sodium benzoate (0·3 g. sodium benzoate to each 50,000 units of aluminium penicillin) were given to 37 patients with pneumonia. The patients received 300,000 units of aluminium penicillin every 12 hours. The authors state that Flippin *et al.* found "higher and more sustained plasma concentrations of penicillin followed aluminum penicillin and benzoate by mouth than any of four other penicillin preparations they tested." It was found that 3½ hours after oral aluminium penicillin the plasma penicillin level was as high as that achieved with intramuscular injection of the same dose of sodium penicillin.

All 37 patients recovered, though 3 had parenteral penicillin before they did so. However, none of them was severely ill at the outset, so oral aluminium penicillin cannot be said to be completely effective in all cases of pneumococcal pneumonia. It is suggested that severe cases will probably be best treated with initial parenteral penicillin followed by oral penicillin (see Abstract 262).
John Forbes

264. **Treatment of Friedländer's Pneumonia**
R. J. GILL. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **221**, 5–9, Jan., 1951. 6 refs.

Among 2,000 cases of pneumonia of all kinds treated in Pennsylvania Hospital during the years 1938 to 1949 there were 25 cases of Friedländer's pneumonia with an over-all mortality of 40%.

There were 3 chronic cases: one patient, treated with sulphonamides and streptomycin, improved; another ran the gamut of drugs with little effect; the third received no specific treatment and died 1½ years later with a non-specific bronchopneumonia. Of the 22 acute cases, 11 were treated with sulphonamides and only 3 died, while the 5 given penicillin all died; 4 received streptomycin with either a sulphonamide or penicillin and all recovered; no patient received streptomycin

alone. In most cases [no figures given] cavities healed and progressive fibrosis did not occur.

The importance of rapid and accurate diagnosis and early administration of the correct specific drugs, sulphonamides and streptomycin, is stressed.

A. Gordon Beckett

265. **A Peculiar Pneumonia associated with Retinal Cytoid Bodies**

P. A. TUMULTY, M. BERTHRONG, and A. MCG. HARVEY. *Bulletin of the Johns Hopkins Hospital* [*Bull. Johns Hopk. Hosp.*] **88**, 239–263, March, 1951. 19 figs., 19 refs.

A report is given of 3 cases of a fatal disease not apparently hitherto described. Two of the patients were women, two were negroes, and all were middle-aged. In each case the illness began insidiously and ran its course to a fatal termination in 3 to 6 months. The first patient sought medical advice because of psoriasis, but admitted later that he had been losing weight and had joint pains with increasing dyspnoea on exertion. The other 2 patients started with an influenza-like illness which went on to a persistent fever with malaise, cough, dyspnoea, and loss of weight.

The clinical course of the illness after admission to hospital was much the same in all cases. Fever persisted throughout (101° to 103° F. (38·3° to 39·4° C.)), cough continued, dyspnoea became progressively worse, cyanosis developed and deepened. In 2 patients there were severe joint pains without objective signs, and in 2 there was terminal evidence of neurological involvement (convulsions and aggressive disorientation). Marked tachycardia became a feature as the dyspnoea intensified. The chief physical signs were found in the chest, where there were constant basal rales and sometimes evidence of pleurisy and pulmonary consolidation. In one patient there was generalized lymph-node enlargement. In all cases cytoid bodies (" cotton-wool spots ") about one-fifth the diameter of the optic disc were visible in the optic fundi.

Exhaustive investigations were carried out on all patients, but without conclusive results. Radiographs of the chest showed soft infiltration spreading gradually throughout the lungs. The leucocyte count remained normal throughout the illness. Electrocardiography showed abnormally low T waves. One patient had a markedly raised, and a second patient a slightly raised, plasma globulin level. Extensive bacteriological investigations failed to reveal a causative agent, though in 2 cases the titre of agglutinins against streptococcus MG rose and then fell during the course of the illness. Treatment in all cases proved unavailing. All available antibiotics were useless, and although one patient improved temporarily on ACTH, she relapsed at once when the drug was discontinued because of excessive fluid retention. Further ACTH then failed to help.

The necropsy findings are described in detail. The principal abnormalities were found in the lungs, in which hardly any normal tissue could be demonstrated. There were widespread acute lesions characterized by marked oedema and haemorrhage in the alveoli and interstitial tissues, thick eosinophilic hyaline membranes lining the walls of many alveoli, mild mononuclear-cell reaction, and relative absence of polymorphonuclear leucocytes. In addition, a striking feature was the widespread presence of organizing alveolar exudate, organizing bronchiolitis, and extensive metaplasia of bronchiolar epithelium. The retinae showed curious cell-like bodies with a central eosinophilic globule in the nerve-fibre layer. Other organs were essentially normal.

The authors draw attention to the similarity between their pathological findings and those seen in fatal cases of virus infections such as ornithosis and atypical pneumonia. Similar organization of alveolar exudates, though much less in degree, may sometimes be seen in these diseases. Some of the pathological features of the authors' cases have also been described in the so-called anaphylactoid pneumonias of acute rheumatism and disseminated lupus erythematosus, in exposure to chlorine and phosgene, and in beryllium poisoning. It is suggested that the present illness may have been a virus pneumonitis of peculiar and chronic type, during which widespread fibrous organization of the lungs took place. Alternatively, it might have been an unusual form of localized collagen vascular disease.

The authors add a note on retinal cytoid bodies, pointing out that they may occur in a variety of apparently unrelated disorders and that their nature and significance is obscure.

John Forbes

266. **Exfoliative Cytology. An Adjunct in the Diagnosis of Bronchiogenic Carcinoma**

E. JACKSON, F. BERTOLI, and L. V. ACKERMAN. *Journal of Thoracic Surgery* [*J. thorac. Surg.*] **21**, 7–23, Jan., 1951. 22 figs., 20 refs.

As an aid to the diagnosis of bronchial carcinoma where a positive biopsy has not been obtained, examination of the sputum or of bronchial aspirations is now widely used. Fresh, early morning specimens of sputum, at least three if possible, are preferred as they give more accurate results than specimens obtained by aspiration at bronchoscopy. The material is smeared on slides, fixed, stained, and examined. Positive results are more often obtained with early or operable tumours; on the other hand, bronchoscopic biopsy is more likely to be helpful in advanced cases.

The authors give their results in examining 270 cases, 100 of which were of carcinoma of the bronchus, the diagnosis being subsequently established by other means. Of these 61 had a positive smear, and 8 a suspicious one. There were thus 31 false-negative results, partly due to inadequacy or unsuitability of the specimens received. In addition, there were 4 false positives. The cells seen in these cases, resembling malignant cells but in fact from chronic inflammatory conditions, are derived from areas of squamous metaplasia. It was not possible to identify the type of carcinoma concerned in the positive cases.

[No mention is made of the pioneer work done on this subject in Britain many years ago. There are several excellent photomicrographs, but the features diagnostic of carcinoma cells are not described.]

M. Meredith Brown

Digestive Disorders

267. **Occupational Factors in the Aetiology of Gastric and Duodenal Ulcers with an Estimate of their Incidence in the General Population**
R. DOLL and F. A. JONES. *Medical Research Council. Special Report Series* [*Spec. Rep. Ser. med. Res. Coun., Lond.*] No. 276, 1–96, 1951. 3 figs., bibliography.

268. **Potassium Deficiency in Idiopathic Steatorrhoea**
M. LUBRAN and P. M. MCALLEN. *Lancet* [*Lancet*] **1**, 321–322, Feb. 10, 1951. 2 figs., 11 refs.

269. **The Affective Response of a Patient with Chronic Ulcerative Colitis to Cortisone**
T. E. MCKELL, S. W. TUTHILL, and A. J. SULLIVAN. *Gastroenterology* [*Gastroenterology*] **17**, 20–24, Jan., 1951. 13 refs.

In a 35-year-old married woman, who was " an example of a typical personality type " such as has been described in patients with chronic ulcerative colitis, the colitis, pyrexia, and general condition steadily worsened in spite of intensive therapy, including the administration of antibiotics. Upon the administration of cortisone, in doses of 100 mg. every 8 hours on the first day, 100 mg. every 12 hours on the second day, and 100 mg. daily for the next 10 days, a striking improvement in " responsiveness, affect and mood " was observed as from the third day; this was followed, as from the eighth day, by satisfactory improvement in the diarrhoea, pyrexia, and vital signs and proctoscopic appearance of the colon. Improvement was maintained after the cortisone was discontinued, and the remission was still complete after 6 months.

The point of this report is that " the beneficial response was first manifested in the personality ". [It should be noted, however, that " the possibility of a miraculous remission was suggested to the patient " before treatment.] *Joseph Parness*

270. **The Effect of ACTH on Nonspecific Ulcerative Colitis**
H. R. ROSSMILLER, C. H. BROWN, and J. A. ECKER. Gastroenterology (*Gastroenterology*] **17**, 25–27, Jan., 1951. 1 fig., 4 refs.

In 5 patients suffering from diarrhoea, pyrexia, and the usual toxic manifestations of an acute exacerbation of chronic ulcerative colitis the usual measures, including the administration of antibiotics, had given no response. Upon the administration of ACTH in doses of 25 mg. every 6 hours for 10 days a fall in temperature to normal occurred in 3 patients, but without improvement in diarrhoea or in the appearance of the rectal mucosa; in 1 case the subsidence of the temperature to normal was accompanied by improvement in the diarrhoea and in the appearance of the rectal mucosa; in 1 patient (who had a low-grade pyrexia) there was no reduction of temperature, nor was there improvement in diarrhoea or in appearance of rectal mucosa.

ACTH appears to be effective in reducing the febrile reaction in acute toxic ulcerative colitis. *Joseph Parness*

271. **Observations on Portal Cirrhosis with Ascites**
W. E. RICKETTS. *Annals of Internal Medicine* [*Ann. intern. Med.*] **34**, 37–60, Jan., 1951. 13 figs., bibliography.

The author reports a study of the plasma protein concentration in untreated cases of portal cirrhosis, and of the effect of medical treatment on the concentration of plasma proteins, on ascites, and on the course of the disease. A comparison was made of 50 patients suffering from portal cirrhosis with 20 healthy controls.

Plasma albumin levels in patients with cirrhosis and ascites were consistently below 3 g. per 100 ml., while those of the normal controls and the patients with cirrhosis but without ascites exceeded this figure. One factor contributing to this low albumin level was insufficient intake of food, and a diet containing 120 g. protein, 350 to 400 g. of carbohydrate, and 3,000 to 5,000 Calories, supplemented by 6 g. of choline chloride, increased the plasma protein level and eliminated oedema and ascites—though such protein changes sometimes required several months to become evident. In addition it was vital in treatment to limit the daily sodium intake, and the author gives details of the effect of sodium restriction in cases with ascites, showing the disappearance of oedema and ascites without the use of diuretics, even though several months' treatment might be needed to obtain this result. He [rightly] emphasizes the need to restrict the sodium intake, especially after paracentesis has been performed, partly because large amounts of protein are lost in the ascitic fluid. If salt is restricted fluid retention can be largely controlled. The elimination of ascites by this means refutes the theory that the ascites is due to fibrosis in the liver, with portal hypertension and stasis. *Thomas Hunt*

272. **Induced Hypoprothrombinaemia as a Test of Liver Function.** (L' épreuve de l'hypoprothrombinémie provoquée chez les hépatiques)
R. DELLA SANTA and K. N. V. KAULLA. *Sang* [*Sang*] **22**, 11–23, 1951. 7 figs., 18 refs.

Details are given of a test of liver function depending upon the degree of hypothrombinaemia produced by " tromexan ". The degree to which prothrombin is reduced is regarded as a direct indication of the functional state of the liver cell. It is emphasized that this test alone gives insufficient information. *A. Piney*

See also Section Radiology, Abstract 116.

Endocrine Disorders

273. **Therapeutic Effect of Subsequent Pregnancy in Simmonds' Disease. Case Report**
R. MURDOCH and A. D. T. GOVAN. *Journal of Obstetrics and Gynaecology of the British Empire* [*J. Obstet. Gynaec. Brit. Emp.*] **58**, 18–21, Feb., 1951. 1 fig., 4 refs.

The case is presented of a patient who developed Simmonds's disease following a post-partum haemorrhage after the birth of her fourth child and her fifth pregnancy. The symptoms were mild, yet severe enough to bring her to hospital, where investigations yielded sufficient evidence to warrant a diagnosis of Simmonds's disease—absence of lactation, amenorrhoea, lassitude, weakness, feeling of cold, and loss of libido, together with wasting, low blood pressure, bradycardia, genital atrophy, loss of hair, increased reaction to insulin, and diminished urinary output of steroids.

Treatment was started with two injections of 1,000 units of serum gonadotrophin followed by 100 units of chorionic gonadotrophin daily for 4 days A further course of treatment was given 6 months later. She showed a slow but steady improvement with some return of menstruation, but ceased attending hospital and was not seen again until she had entered upon her sixth pregnancy some 4 years later. Her confinement was normal, but was followed by absence of lactation as after the previous pregnancy. Her general condition improved very greatly after this and her symptoms and signs disappeared. *D. M. Stern*

274. **The Mechanism of Polyuria of Diabetes Insipidus in Man. The Effect of Osmotic Loading**
W. A. BRODSKY and S. RAPOPORT. *Journal of Clinical Investigation* [*J. clin. Invest.*] **30**, 282–291, March, 1951. 3 figs., 35 refs.

275. **A Case of True Hermaphroditism**
A. W. CAPON. *Lancet* [*Lancet*] **1**, 563–565, March 10, 1951. 7 figs., 3 refs.

EXPERIMENTAL ENDOCRINOLOGY

276. **Effect of Commercial Cortisone Acetate Suspension on Capillary Permeability**
V. MENKIN. *American Journal of Physiology* [*Amer. J. Physiol.*] **164**, 294–300, Jan., 1951. 1 fig., 11 refs.

Commercial cortisone acetate suspension injected intracutaneously into rabbits in amounts ranging from 0·5 to 2·0 mg. produced increased capillary permeability at the site of injection. By injecting in a similar way comparable amounts of different cortical extracts or substances used for the suspension of these preparations, the author has demonstrated that the increase in capillary permeability was due solely to the material used as the vehicle for the cortisone, probably some type of alcohol. Adrenocorticotrophic hormone (ACTH) produced no such effect. Cortisone acetate, free from any alcohol or vehicle, failed to increase capillary permeability when suspended in saline. This effect on the capillaries may possibly help to elucidate the action of cortisone acetate suspension in arthritic conditions, and this additional variable, the author believes, will have to be taken into account in future clinical studies.
A. I. Suchett-Kaye

277. **Enhancing Effect of Cortisone upon Poliomyelitis Infection (Strain MEF1) in Hamsters and Mice**
G. SHWARTZMAN. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 835–838, Dec., 1950. 13 refs.

Intramuscular doses of adrenocorticotrophic hormone (ACTH) and/or cortisone (5 mg. of each) were given to male Swiss mice weighing 10 to 14 g. and male hamsters weighing 22 to 27 g. in groups of 9 to 21 animals. The virus was maintained by serial intracerebral passage in mice and its identity checked periodically by neutralization tests with anti-Lansing monkey serum. The intracerebral inoculation dose for both animal species was 0·05 ml. of the brain emulsion, suitably diluted with saline. All surviving animals were examined daily for a period of one month.

Intracerebral inoculation of the virus in mice given cortisone and ACTH 2 hours previously was followed by a shortening of the incubation period and correspondingly earlier mortality compared with the controls. Intraperitoneal injection of the virus did not produce this effect.

In hamsters the effect was more striking. Previous experiments showed that these animals were normally quite resistant to intracerebral inoculation of poliomyelitis virus. After pretreatment with cortisone or ACTH and cortisone, what is normally a mild infection with small mortality rate became a rapidly progressing, violent, and uniformly fatal disease. ACTH alone failed to produce this effect, possibly, the author suggests, because of the elaboration of an unknown factor capable of reversing the enhancing effect of cortisone.
Norval Taylor

278. **Role of Cortisone in Regulation of Inflammation**
T. F. DOUGHERTY and G. L. SCHNEEBELI. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 854–859, Dec., 1950. 4 figs., 21 refs.

The authors describe their investigations into the histology of experimentally induced allergic and traumatic inflammation in adrenalectomized and adrenalectomized and cortisone-treated mice. Adrenal cortical secretions and exogenous cortisone were shown to inhibit inflammation without interfering with the antibody–

antigen reaction. [As this paper is not readily abstracted, the original should be consulted for the technical details.] *Norval Taylor*

279. **A Method for Detecting Cortisone in Body Fluid**
C. L. COPE. *British Medical Journal* [*Brit. med. J.*] **1**, 271–272, Feb. 10, 1951. 1 fig., 6 refs.

A simple method is described for the extraction of cortisone-like material from urine. The material is injected into adrenalectomized mice and its effect on the number of circulating eosinophil cells is measured. Preliminary results showed that cortisone-like activity was absent from the urine of patients with Addison's disease and hypopituitarism, but increased during ACTH administration, in late pregnancy, and in a patient with an adrenal cortical carcinoma. *A. C. Crooke*

280. **Failure of Adrenalectomy Immediately Following Stress to Prevent Eosinopenia in Rats**
W. D. LOVE. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 639–641, Dec., 1950. 1 fig., 7 refs.

Male and female albino rats of the Fairfield strain, weighing 125 to 250 g., were used. The animals received 0·2 mg. adrenaline per kg. subcutaneously and were then restrained in a tail cage for 4 hours. Eosinophil counts were made by a modification of the Randolph technique (*J. Allergy*, 1944, **15**, 89) on tail blood at 10 minutes, 2 hours, and 4 hours after the injection. A total of 0·57 c.mm. blood was counted in aqueous 50% propylene glycol with 0·1% eosin.

Single-stage adrenalectomy was performed under ether, the time required to complete the operation being measured from the time the animal was first picked up to the clamping of the second adrenal pedicle.

It was found that an eosinopenia followed stress even though adrenalectomy was complete within 10 minutes, and that the continued normal 4-hour fall in circulating eosinophils took place in the absence of continued secretion by the adrenal cortex. *Norval Taylor*

281. **Liberation of Adrenaline from the Suprarenal Gland of the Rabbit**
G. B. WEST. *British Journal of Pharmacology and Chemotherapy* [*Brit. J. Pharmacol.*] **5**, 542–548, Dec., 1950. 1 fig., 13 refs.

By means of parallel biological assays the amounts of adrenaline and noradrenaline in the adrenal glands of the rabbit and in adrenal venous blood before and during splanchnic stimulation were estimated. Adrenal glands were taken after death, the capsule removed, and the gland ground with sand and 10 ml. 0·1N hydrochloric acid per g. The extract was filtered and assayed. Adrenal blood was collected, in eviscerated rabbits anaesthetized with urethane, from a cannula in the vena cava between ligatures which closed all veins other than the left adrenal vein. The blood was rapidly cooled and centrifuged and the plasma assayed.

The tests employed were on: (1) fresh rabbit ileum, which was twice as sensitive to adrenaline as to noradrenaline (A/N ratio 0·5); (2) rabbit ileum stored 4 days at 4° C. (A/N ratio 3·0); (3) blood pressure of rabbit anaesthetized with urethane, treated with cocaine 8 mg. per kg., and with the vagi cut (A/N ratio 0·5); (4) isolated rectum of week-old chick (A/N ratio 0·05); (5) isolated uterus of rat in dioestrus (A/N ratio 0·02).

The sympathin obtained was principally adrenaline. This was the case with sympathin extracted from the gland and also with that from the adrenal venous blood. In 10 rabbits when the left gland was stimulated before it was removed the mean concentration of adrenaline was 568 mg. per g. compared with 418 mg. per g. in the right (range 400 to 890 mg. and 225 to 756 mg. respectively). In 9 rabbits where neither gland was stimulated the means were: left 472, right 498 mg. per g. Noradrenaline was detected only twice, each time in unstimulated glands and amounting to about 10% of the total sympathin. In 12 rabbits the mean adrenaline concentration in plasma from the adrenal vein was 0·084 mg. per ml. Noradrenaline was detected in plasma from 3 of the rabbits in concentrations of 0·02, 0·01, and 0·03 mg. per ml. During splanchnic stimulation the amount of adrenaline rose and noradrenaline was detected more often. The amount of noradrenaline was greatest in the samples collected between the 9th and 12th minutes of stimulation, when the percentage of adrenaline fell to 68. Adrenaline only was detected after the 15th minute of stimulation. *R. P. Stephenson*

282. **Effects of Thyroidectomy and of Thiouracil on Adrenal Weight and Ascorbic Acid**
H. H. FREEDMAN and A. S. GORDON. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **75**, 729–732, Dec., 1950. 2 figs., 13 refs.

The administration of 0·2% thiouracil in the diet, or surgical thyroidectomy, caused pronounced atrophy in the adrenal glands of young male rats, the atrophy being less marked when thyroidectomy was performed. Adrenal ascorbic acid content increased initially in the thiouracil-treated and in the operated animals, followed by a return to normal values in the former group, while in the thyroidectomized rats there was a final decrease in ascorbic acid concentration. Both types of hypothyroidism could be prevented by the subcutaneous injection of 5·0 μg. thyroxine daily. It was concluded that changes in adrenal size influence the reliability of the adrenal ascorbic acid content as an index of cortical activity. *Norval Taylor*

THYROID AND PARATHYROID

283. **Familial Types of Thyrotoxicosis and their Relation to Tuberculosis.** (États basedowiens de caractère familial et tuberculose).
P. DELORE and G. NOEL. *Presse Médicale* [*Pr. méd.*] **59**, 245–246, Feb. 24, 1951.

Earlier observations indicated a relation between tuberculosis and familial thyrotoxicosis. The present authors report 10 further cases of thyrotoxicosis, in

all of which another member of the family showed thyroid dysfunction, and in 6 of which there was a family history of tuberculosis. They consider that thyroid disease is often the result of a tuberculous lesion, and that a systematic search would reveal tuberculosis in the families of two-thirds of all thyrotoxic patients.

Nancy Gough

284. **Endemic Goitre in North-east Switzerland. Results of 27 Years' Prophylaxis with Iodized Salt.** (Die Kropfendemie in der Nordostschweiz. Ergebnisse einer 27 jährigen Jodsalzprophylaxe)
M. RICHARD. *Praxis* [*Praxis*] **40**, 1–6, Jan. 4, 1951. 4 figs., 11 refs.

This article records the striking effect of iodized salt on the incidence of goitre in the various cantons of Switzerland. The incidence of goitre among children in 1922 was as high as 65% in some parts, and where prophylaxis has been carefully carried out this has fallen to below 5%. There still appears to be a deficit of 100 μg. out of the daily need of 200 μg. in the iodine intake of many of the population, but, despite this, goitre is becoming less common. Army discharges due to goitre have fallen from 64% in the 1900 to 1905 period to 0·7% in 1944 to 1947. Iodine lack is not the only factor in the production of goitre, and vitamin A is important in this connexion. The post-operative relapse rate of goitre is reduced by the administration of iodine to all patients operated on for goitre, but it is not entirely abolished; it is possible that lack of vitamin A is responsible for these relapses. In the future it is hoped that the iodine content of salt will be increased to give an adequate daily iodine intake, and that animal manure will replace chemical fertilizers, because the former has been shown to increase the vitamin-A content of fodder and vegetables.

G. S. Crockett

285. **Observations on a Case of Idiopathic Hypoparathyroidism**
A. JORDAN and A. R. KELSALL. *Archives of Internal Medicine* [*Arch. intern. Med.*] **87**, 242–258, Feb., 1951. 7 figs., 46 refs.

A case of idiopathic hypoparathyroidism is described. The main clinical features were chronic tetany, epileptoform attacks, stunted growth, retarded eruption of teeth, early bilateral cataracts, and symmetrical intracerebral calcification. The serum calcium level and urinary calcium excretion were low. The serum inorganic phosphorus level was high, and the serum alkaline phosphatase activity was increased. No cause for the condition was found.

Initial treatment with calcium lactate and large doses of calciferol was without effect on the condition, but an increase in the protein intake, together with the continued administration of calcium lactate and calciferol, was followed by disappearance of the tetany and a return to normal of the serum calcium. Before treatment, a balance experiment showed that the patient was in slightly positive calcium balance and more markedly negative phosphorus balance. A second balance experiment, when treatment had become effective, showed a considerable increase in the amount of calcium retained, but the loss of phosphorus continued at a higher rate. The return of the serum calcium to normal was associated with a fall in the serum inorganic phosphorus and a diminution in the serum alkaline phosphatase activity.

Fourteen months after the initial correction of the hypocalcemia there had been no return of tetany and no further epileptiform attacks; normal serum calcium levels were being maintained with administration of calcium chloride and calciferol, although the protein intake has been allowed to revert to normal. There was little change in the teeth; the intracerebral calcification was apparently unchanged, but there was some evidence of regression of the cataracts in both eyes.—[Authors' summary.]

286. **The Biochemical Changes in Recklinghausen's Disease of the Skeleton**
S. V. TELFER. *Glasgow Medical Journal* [*Glasg. med. J.*] **32**, 59–71, March, 1951. 11 refs.

Figures are presented showing changes in blood and urinary constituents in 7 women with Recklinghausen's disease, before and after operation. The estimations included calcium and phosphorus content of the serum, sodium chloride content and carbon dioxide combining power of the plasma, and acidity level, ammonia coefficient, and calcium content of the urine.

Before operation the calcium level was raised in 5 of the 7 cases (11 to 14 mg. per 100 ml.), with a slight reduction in serum phosphorus level and increased excretion of both elements; all cases showed a raised ammonia coefficient and lowered carbon dioxide combining power of the plasma. Plasma chloride levels were normal. Removal of the parathyroid adenoma resulted in a rapid fall in the blood calcium level, accompanied by tetany. Comparison is made with similar determinations in cases of localized osteitis, bone metastases in malignant disease, and myelomatosis.

F. W. Chattaway

ADRENAL GLANDS

287. **Adrenal Cortical Failure following Treatment with Cortisone and ACTH. Report of a Case**
E. L. PROCTOR and A. J. RAWSON. *American Journal of Clinical Pathology* [*Amer. J. clin. Path.*] **21**, 158–162, Feb., 1951. 2 figs., 6 refs.

This is believed to be the first case report of irreversible damage to the fascicular zone of the adrenal cortex following treatment with cortisone and ACTH.

The patient was a negress of 36 who had had lupus erythematosus and chronic cervicitis for 2 years. She was treated with radium for the cervicitis, but became progressively worse, with fever, malaise, weakness, and joint pains. She developed dry, scaly, depigmented areas on the nose, cheeks, and elsewhere, and there was stiffness and atrophy of the interosseous tissues of the hands and feet. All joints were painful on motion. The clinical diagnosis was lupus erythematosus disseminatus.

Cortisone was given in doses of 300 mg. on the first day, 200 mg. on the second day, and 100 mg. daily thereafter for 7 days. Soon after the start of treatment she felt much better and the joint pains had gone. A second course of cortisone was given, but pneumonitis developed and the patient died some 3 weeks later.

At necropsy the main findings were in the adrenal cortex. The cells of the zona fasciculata showed pyknosis of their nuclei and the cytoplasm was largely absent. As the lesions of lupus erythematosus disseminata were relatively inconspicuous in comparison with the marked damage to the adrenal cortex, it was presumed that adrenal cortical failure was the cause of death.

R. B. Lucas

288. **Phaeochromocytoma of Adrenal Gland, with Sustained Hypertension**

H. J. C. SWAN. *British Medical Journal* [*Brit. med. J.*] **1**, 440–444, March 3, 1951. 3 figs., 30 refs.

The case is described of a man of 42 who was admitted to St. Thomas's Hospital, London, with a history of hypertension of at least 8 years' duration, and of attacks of sweating since the age of 16 years. The sweating was restricted to the face and neck, was frequently induced by emotion, and was preceded by a temporary blanching of the skin. Other symptoms included headaches, tiredness, and effort dyspnoea. The blood pressure ranged from 240/140 mm. Hg to 170/110 mm. Hg, and the oral temperature fluctuated around 90° F. (37·2° C.). Renal function was normal, but a radiograph of the abdomen showed calcified opacities above the left kidney. A diagnosis of essential hypertension was made and splanchnic sympathectomy decided upon. At operation, however, a phaeochromocytoma of the left adrenal was discovered and removed. The post-operative hypotensive collapse was controlled by intravenous infusions of L-noradrenaline. One month after operation the blood pressure was 125/80 mm. Hg.

The various tests for the diagnosis of phaeochromocytoma with sustained hypertension are discussed, and attention is drawn to the value of a history of sweating and peripheral vasomotor phenomena and of simple tests such as the response of the cardiovascular system to cold and change of posture, a positive cold pressor test being uncommon and postural hypotension and tachycardia common in cases of phaeochromocytoma.

G. Ansell

289. **Two Cases of Phaeochromocytoma**

K. V. CROWTHER. *British Medical Journal* [*Brit. med. J.*] **1**, 445–448, March 3, 1951. 5 figs., 9 refs.

This paper records 2 cases of phaeochromocytoma. The first was in a man aged 24 who complained of attacks of headache, nausea, and vomiting, with blurring of vision of 16 years' duration. He also suffered from excessive sweating, postural giddiness, and dyspnoea with palpitation on exertion. The blood pressure ranged from 150/100 mm. to 190/135 mm. Hg, being increased by moderate exertion. The left kidney was found to be congenitally deformed and was removed. During the operation the patient developed a hypotensive crisis and died within a few hours from pulmonary oedema and bronchopneumonia. At necropsy an unsuspected phaeochromocytoma replacing the right adrenal gland was found.

The second case was that of a pregnant woman aged 29 who complained of severe frontal and occipital headaches, sweating, and coldness of the hands and feet. The attacks usually occurred on rising from or retiring to bed, and could also be precipitated by exertion. She had had 2 previous unsuccessful pregnancies, a diagnosis of chronic nephritis having been made during the first. The blood pressure ranged from 140/90 mm. to 180/130 mm. Hg, and albuminuria was present. The glucose tolerance curve was of a diabetic type. The right kidney was palpable, and a pyelogram showed a ptosed right kidney with a focus of calcification above this. The diagnosis of phaeochromocytoma was confirmed by a positive benzodioxane test. The tumour was successfully removed surgically, the rise in blood pressure during operation being controlled by " piperoxane " (2 : 1-(1-piperidyl-methyl)-1 : 4-benzodioxane hydrochloride). The blood pressure, urine, and glucose tolerance curve subsequently returned to normal.

G. Ansell

290. **A Case of Adrenal Phaeochromocytoma**

J. F. PANTRIDGE and M. MCC. BURROWS. *British Medical Journal* [*Brit. med. J.*] **1**, 448–449, March 3, 1951. 2 figs., 9 refs.

A woman of 66 had suffered from " peculiar attacks " for at least 7 years. Each attack began with epigastric discomfort and flatulence, followed by " a feeling like an electric shock " in the limbs, back of the neck, and back of the head. Examination between the attacks revealed a blood pressure of 140/80 mm. Hg, left ventricular enlargement, and a palpable swelling in the right kidney region. During an attack the face was flushed, the limbs were trembling, and the hands were cold and cyanosed. The blood pressure was 270/170 mm. Hg and the pulse rate 150. An injection of histamine (0·05 mg.) caused a symptomless rise of blood pressure with no tachycardia. Following the administration of " dibenamine ", histamine failed to cause any rise in blood pressure. A chromaffin-tissue tumour of the right adrenal medulla was diagnosed, and was found and removed at operation. The hypertension caused by handling the tumour was controlled by dibenamine, and the hypotensive collapse which followed the clamping of the tumour pedicle was controlled by the intravenous injection of 40 ml. of a solution of noradrenaline (10 μg. per ml.) and the intramuscular injection of 20 mg. of " methedrine " over a period of 19 minutes. Eight weeks after operation, the blood pressure was 145/100 mm. Hg, the heart size remaining unchanged.

It is suggested that the hypertension without tachycardia produced by histamine may have been due to the release of noradrenaline, and that the spontaneous attacks were associated with the release of adrenaline.

G. Ansell

See also Sections Pathology, Abstract 151 ; Paediatrics, Abstract 174.

Dermatology

291. **Clinical Experiences with ACTH-treatment of Certain Skin Diseases.** [In English]
H. BRODTHAGEN, F. REYMANN, and M. SCHWARTZ. *Acta Endocrinologica (Copenhagen)* [*Acta endocrinol., Kbh.*] **6**, 110–132, 1951. 9 figs., 20 refs.

ACTH had no beneficial effect when given to a patient suffering from periarteritis nodosa and to 4 patients with severe psoriasis. Remarkable improvement in a man of 49 suffering from pemphigus was maintained 3 months after cessation of treatment, but a similar case in a female patient of 68 relapsed whenever the ACTH was withdrawn. There was marked improvement in one patient with diffuse sclerodermia, but no improvement in a second case. Small doses (5 to 45 mg. daily) were given, and it is advised that the treatment should be withdrawn gradually. No serious side-effects were seen, but most patients complained of tiredness and apathy on withdrawal of the drug.

John T. Ingram

292. **The Dermo-epidermal *p*H in Melanogenesis.** (Note sur le *p*H dermo-épidermique dans la mélanogénèse)
F. CAILLIAU. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **78**, 42–47, Jan.–Feb., 1951.

Miescher has shown that the epidermis has an acid and the dermis an alkaline reaction. There is no satisfactory chemical, histological, or physiological explanation of the mechanism of pigmentogenesis. The author suggests that a rational concept of the process may be based on the dermo-epidermal *p*H difference, and likens melanogenesis to a coloured flocculation reaction between colloids with opposite charges.

James Marshall

293. **Mammillaria**
G. O. HORNE and R. H. MOLE. *Transactions of the Royal Society of Tropical Medicine and Hygiene* [*Trans. R. Soc. trop. Med. Hyg.*] **44**, 465–471, Feb., 1951. 5 figs., 8 refs.

In a previous paper by these authors (*Trans. R. Soc. trop. Med. Hyg.*, 1950, **44**, 193; *Abstracts of World Medicine*, 1951, **9**, 277) it was stated that " mammillaria " is always present in cases of anhidrotic heat exhaustion in tropical climates, though patients may suffer from mammillaria without developing heat exhaustion. A description of the former condition is now given, as seen in 66 cases of heat exhaustion at Karachi in 1946 and 1947. The affected skin was studded with pale, circular, closely packed, firm elevations about 1 mm. in diameter. These elevations were uniform and only the degree of prominence or the size of the affected area varied in different patients or at different times. They were seen mostly over the thorax, though in severe cases they spread over the limbs and the face. They evolved from prickly heat, but they were thought not to be the cause of absence of sweating in these cases since: (1) sweating was often present where there was mammillaria and increased in adjoining areas; (2) the elevations did not appear to be situated over sweat ducts; and (3) the elevations did not contain fluid which might have come from blocked ducts. Although the authors claimed that skins affected by mammillaria often felt rough " like studs of a nutmeg grater " [an expression frequently used in the description of hyperkeratosis] and although they saw mild mammillaria in people who had never been in the tropics, they concluded that mammillaria was a condition distinct from " permanent gooseflesh ".

[It seems probable from their description and photographs that the authors were, indeed, not dealing with hyperkeratosis, because the latter consists of spiky rather than rounded elevations, it is seldom seen on the chest, and it is associated with cold skins. Histological examination of biopsy specimens of the skin of persons affected by mammillaria and their comparison with specimens of normal and hyperkeratotic skin from corresponding regions of the body surface would seem valuable.]

E. M. Glaser

294. **Aetiology of Argyria.** (Note sur l'étiologie des argyries)
B. DUPERRAT. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **78**, 36–41, Jan.–Feb., 1951. 40 refs.

Argyria may be general or local; the local variety may result from local applications or, more rarely, from absorption of silver from a different surface. The various silver compounds which may cause argyria and their methods of use are detailed. The author points out that no other type of intoxication demonstrates better the factor of individual sensitivity, as there is no relationship from case to case between dosage and time of application and the development of pigmentation.

James Marshall

295. **Further Studies on the Mechanism of Adhesive Tape Dermatitis**
S. M. PECK, T. J. MICHELFELDER, and L. L. PALITZ. *Archives of Dermatology and Syphilology* [*Arch. Derm. Syph., Chicago*] **63**, 289–311, March, 1951. 11 figs., 20 refs.

A fleeting reaction may follow removal of adhesive tape as a direct result of mechanical injury, but dermatitis may also arise as the result of a specific allergic sensitivity to one of the ingredients of the plaster. The authors are, however, concerned chiefly with a third type of reaction following the application of adhesive tape for 5 days or more, in which no specific sensitiveness can be

demonstrated by patch test. They believe that this reaction is primarily due to a plugging of orifices of sweat ducts by hyperkeratosis according to a mechanism similar to that described in miliaria rubra. A secondary factor may be the multiplication of bacteria which takes place in the macerated skin. *John T. Ingram*

296. **The Nature of the Inclusion Body of Verruca Vulgaris: a Histochemical Study of Nucleotids**
H. BLANK, M. BUERK, and F. WEIDMAN. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **16**, 19–30, Jan., 1951. 10 figs., 18 refs.

The authors review our present knowledge of warts and report the results of an investigation of some of the chemical changes which occur in the infected epithelial cells. A total of 150 warts of various types from 65 patients were examined histologically after staining with haematoxylin and eosin and with pyronine–methyl green. Some were also stained with toluidin blue to demonstrate both ribose and desoxyribose nucleic acids and with Feulgen's stain to demonstrate desoxyribose nucleic acid only.

The only distinctive change noted in the nuclei was an accumulation of basophilic material, when stained with haemotoxylin and eosin, which distended the nuclear membrane and replaced other nuclear structures. This was the inclusion body of Lipschütz and was found in about half of the warts examined. From the staining reactions it appeared that the inclusion material was largely nucleoprotein, chiefly in the form of desoxyribose nucleic acid. As the latter is the chief nucleic-acid constituent of the larger animal viruses, the authors consider that the accumulation of inclusion material containing newly formed desoxyribose nucleic acid is cytological evidence of the aggregation of wart virus in the nuclei of epithelial cells. *S. T. Anning*

297. **Recurrent Kaposi's Varicelliform Eruption in an Adult**
W. C. BOAKE, J. A. DUDGEON, M. BURNET. *Lancet* [*Lancet*] **1**, 383–384, Feb. 17, 1951. 13 refs.

298. **Role of Sulphonamides and Penicillin in the Pathogenesis of Systemic Lupus Erythematosus**
S. GOLD. *Lancet* [*Lancet*] **1**, 268–272, Feb. 3, 1951. 40 refs.

The author describes in detail the clinical progress of a series of 8 cases of systemic lupus erythematosus at St. George's Hospital, London. All these patients were seen within a period of 6 months; all but one had received penicillin or one or more courses of sulphonamides before their lupus erythematosus became systemic, and on the two occasions on which sulphonamides had been administered after dissemination the effect was bad. Of 4 patients who were given penicillin after admission to hospital, in 3 the condition deteriorated immediately; all 4 died. Of the whole series of 8 patients, 5 are now dead and in 3 the disease is in a subacute phase.

The opinion of the author is that in a hypersensitivity disease the use of drugs known to be sensitizers should be avoided. *H. S. Laird*

299. **Urticaria following Adrenaline but not Noradrenaline**
H. HERXHEIMER. *Lancet* [*Lancet*] **1**, 615, March 17, 1951. 1 ref.

300. **Fifty Years of Parapsoriasis.** (Le cinquantenaire du parapsoriasis)
A. CIVATTE. *Annales de Dermatologie et de Syphiligraphie* [*Ann. Derm. Syph., Paris*] **78**, 5–22, Jan.–Feb., 1951. 11 figs.

An excellent clinical and histological review of parapsoriasis is given, in which the author clearly dissociates parapsoriasis *en gouttes* from the lichenoid and plaque forms. In the last two forms the histological picture is similar and the changes are chiefly dermal; in the first the changes are mainly epidermal. Moreover, transitional forms occur between the lichenoid and plaque varieties, but never between the guttate variety and the two others. He suggests the identification of a particular transitional form between parapsoriasis lichenoides and parapsoriasis *en plaques* under the name of "parapsoriasis *en plaques avec papules*".

[This important article should be read in the original.] *James Marshall*

301. **Pituitary Adrenocorticotropic Hormone (ACTH) and Cortisone in Diseases of the Skin. I. Pemphigus Vulgaris and Other Bullous Dermatoses**
A. B. CANNON, J. G. HOPKINS, G. C. ANDREWS, H. F. COLFER, P. GROSS, C. T. NELSON, and C. M. HOWELL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **145**, 201–206, Jan. 27, 1951. 6 figs., 10 refs.

The authors list 9 skin conditions in which, according to published reports, pituitary adrenocorticotrophic hormone (ACTH) may be beneficial, and 7 in which it appears to be ineffective or even detrimental. In the present paper they report the effects of ACTH treatment in 11 cases of bullous dermatosis of various types seen at the Columbia-Presbyterian Medical Center, New York.

In 5 cases of pemphigus vulgaris ACTH therapy was initiated after the disease had been present for periods ranging from one week in one case to one year in another. The first course usually consisted of between 60 to 100 mg. daily for 3 to 20 days and in every case produced a remission, which was sometimes dramatic; but relapses always occurred on withdrawing the ACTH and the condition responded less well and only to greatly increased dosage in subsequent courses until finally new lesions appeared in spite of continued therapy. One of these patients died of fulminating pemphigus and another of mesenteric thrombosis, which was possibly due to co-existing Buerger's disease or to the effect of ACTH itself.

Two patients with pemphigus vegetans were also treated, both patients undergoing great clinical improvement and being discharged on a maintenance dose of about 100 mg. of ACTH a day; one of them has actually returned to work. Of 2 cases of erythema multiforme pemphigoides, temporary clinical cure was obtained in one with an 11-day course of 100 mg. of

ACTH daily, followed after 6 months by a course of weekly injections of 50 mg. of cortisone acetate. The other patient, after initial improvement on a dose of 80 mg. of ACTH daily, decreasing to 40 mg. daily, relapsed 5 weeks after stopping the treatment, but again responded well to 40 mg. ACTH daily for 14 days. He has since been lost sight of. (In these 2 cases there was some difference of opinion concerning the diagnosis.) Two patients with epidermolysis bullosa of the congenital dystrophic type showed no objective improvement on treatment with cortisone acetate, although appetite and sense of well-being improved.

In all 11 cases the blood pressure was initially low (96 to 108 mm. Hg systolic) and rose to normal levels on treatment. The frequent association with pemphigus of degenerative or necrotic lesions of the adrenal cortex and disturbances of serum electrolyte content is pointed out, although only in 4 of the present series was any abnormality of the blood chemistry, in the form of slightly diminished serum sodium content, found. ACTH and cortisone appear to produce identical effects, namely, easier management of the case, restoration of serum electrolyte balance, improvement of systolic blood pressure and gain in weight.

Ferdinand Hillman

302. **A Clinical and Pathogenetic Study of Hyalinosis Cutis et Mucosae.** (Beitrag zur Klinik und Pathogenese der Hyalinosis cutis et mucosae (Lipoid-Proteinose Urbach–Wiethe))

K. H. HOLTZ and W. SCHULZE. *Archiv. für Dermatologie und Syphilis* [*Arch. Derm. Syph., Wien*] **192**, 206–237, 1951. 20 figs., bibliography.

Hyalinosis cutis et mucosae, of which 32 cases have been reported in the literature since 1908, is a slowly progressive condition which is frequently familial. The mucosae of the mouth and upper respiratory tract show rows of variously sized, diffuse, yellow-white nodules. Involvement of the glottis produces hoarseness, and the inability to cry is often the presenting symptom in a child. Tracheotomy may become necessary. Other mucosae are more rarely involved. The skin manifestations usually appear later and comprise: (1) Slight infiltration and diffuse, pale yellow discoloration followed by lichenoid, moderately coarse nodules of pin-head to lentil size. (2) Confluence of these nodules and penetration into the deeper layers may produce cushion-like excrescences, spongy to touch. This renders the normal skin folds much more prominent. (3) On pressure points, such as on the palms, thickly set, hyperkeratotic papules may produce a sandpaper-like surface. (4) Depigmented, atrophic skin areas are scattered among the other lesions.

Three cases seen at the Freiburg University Skin Clinic are described in great detail. The first 2 patients came of a family of 6 children of whom 4 (all male) were affected. One of these two suffered from epileptiform convulsions, and a radiograph of the skull showed suprasellar calcifications such as have not previously been described in the German literature. The third case was in a female whose only brother was unaffected, as were her parents, who were first cousins, and her daughter. It is suggested that the condition is transmitted as a Mendelian recessive character.

The histology of specimens of the homogeneous masses from many affected areas was studied in preparations stained by a variety of techniques, and the significance of the results are discussed. The lesions were also investigated from the histochemical aspect in 2 of the cases. Cholesterol esters were found in the deposits, so that the presence of pure phosphatides could be excluded, and it was found that the fat contained in the deposits was only partly soluble in cold absolute alcohol but readily in cold acetone. The phospholipid content of the affected areas of skin was about twice that of normal controls, but the serum phospholipid level was subnormal in one case and normal in the other. In both the cases there was an increase in the level of α- and β-globulin in the serum, and a decrease in the albumin level.

The authors discuss the question of pathogenesis—as to whether a disturbance of lipid or protein metabolism is responsible for the development of the condition, or whether the condition is due to increased capillary permeability, or possibly an endocrine disturbance leading to a change in plasma colloid composition.

[Many photographs are reproduced which convey a very good impression of the lesions, while the radiographs showing intracranial calcification, which are also reproduced, are very striking.] *Ferdinand Hillman*

303. **Experimental Miliaria in Man. IV. Sweat Retention Vesicles following Destruction of Terminal Sweat Duct**

W. B. SHELLEY. *Journal of Investigative Dermatology* [*J. invest. Derm.*] **16**, 53–64, Jan., 1951. 7 figs., 15 refs.

Simple mechanical obstruction of the sweat duct may, in the presence of sweating, produce cutaneous changes which vary in type according to the level at which sweat retention occurs. Retention of sweat in the stratum corneum appears clinically as asymptomatic miliaria crystallina; if lower in the epidermis, as miliaria rubra; and if in the dermis, as asymptomatic papules (miliaria profunda). An attempt was made to produce sweat retention in the dermis experimentally by electrolytic injury of sweat ducts stained with methylene blue by iontophoresis. This was carried out in 16 healthy white males in whom sweating was induced 2 to 30 days later by means of an infra-red heating cabinet. The treated ducts were anhidrotic when general sweating was induced, and small papules appeared at the sites of treatment. On pricking them fluid was released, suggesting that they were vesicles. Involution of the vesicles occurred with cooling, and re-appearance on further heating. Local injection of atropine prevented their appearance. The papules or vesicles were investigated histologically and four types of sweat retention were identified: in a papulo-vesicle in the stratum corneum, in an intra-mid-epidermal papulo-vesicle, in a dermal papulo-vesicle just beneath the epidermis, and as a simple retention of sweat within the dermis without any clinical signs or symptoms. *S. T. Anning*

Venereal Diseases

304. Aureomycin Therapy in Lymphogranuloma Venereum

A. FLETCHER, M. M. SIGEL, and H. A. ZINTEL. *Archives of Surgery* [*Arch. Surg., Chicago*] **62**, 239–250, Feb., 1951. 28 refs.

The authors, in treating a group of 19 cases of lymphogranuloma venereum with aureomycin at the University of Pennsylvania Hospital, had three objects in view: (1) to study the effectiveness of aureomycin when administered orally; (2) to observe the clinical course of the patients for a period of months after treatment; and (3) to study the effect of treatment on the persistence of complement-fixing antibodies in the blood serum. The dosage of aureomycin given orally was 2·0 g. daily for 7 or, later on, 28 days, nausea and vomiting making it necessary in some cases to reduce this to 1·0 g. daily or even to discontinue it; the dosage given intramuscularly was 20 mg. daily for 10 days. The patients were subdivided into four groups: (1) acute inguinal adenitis; (2) proctitis without stricture; (3) rectal stricture without colostomy; and (4) rectal stricture with colostomy.

There were 3 patients in the first group, in each of whom the buboes subsided within 2 weeks of the start of treatment. They were followed up for periods of 8 to 11 months, 2 of the 3 (treated orally) remaining symptom-free and showing a marked and progressive fall in the titre of complement-fixing antibodies in their serum. The third patient, who was treated with intramuscular aureomycin, showed no definite decrease in titre and had a mild recurrence of adenitis 2 weeks after stopping treatment. In the second group there were 2 patients, one of whom was treated with intramuscular aureomycin on two occasions and the other with chloramphenicol, 3 g. daily by mouth for 28 days. In the first patient clinical improvement began after 2 days of treatment; there was complete relief of symptoms for 5 months, but relapse then occurred and further treatment resulted only in slight improvement. The other patient was clinically improved, but proctoscopic examination suggested early stricture formation. In the third group there were 7 patients, all of whom were treated with oral aureomycin, the average total dose ranging from 28 to 70 g. In 2 cases there was no improvement, but in 5 symptomatic relief followed, although objective improvement was less striking. In the fourth group there were also 7 patients, 3 of whom were first treated by intramuscular injection of aureomycin for 10 days, further treatment being then given by mouth, while the remainder were treated entirely with oral aureomycin. Total dosage ranged from 10 to 64 g., and the period of observation from 9 to 12 months. In some cases there was subjective improvement, but there was found to be only slight change in the stricture.

Of the whole group of 19 patients only 2 showed a definite fall in the antibody titre; these were cases of acute inguinal adenitis, the virus apparently surviving treatment in the more chronic infections. The authors feel that a final conclusion concerning the effects of aureomycin must await further observation of these patients over a period of years. *H. S. Laird*

305. Aureomycin in Intractable Non-specific Urethritis

W. MCL. THOMSON. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 149–150, Jan. 27, 1951.

Aureomycin by mouth was given in 6 cases of non-specific urethritis which had failed to respond to sulphonamides, penicillin, and other measures. The symptoms disappeared promptly, but 2 patients relapsed; however, further oral aureomycin cleared up these cases and all were eventually cured. *G. M. Findlay*

306. The Contemporary Male Defaulter

G. O. HORNE. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **26**, 164–171, Dec., 1950. 1 ref.

This thoughtful report analyses the behaviour in respect of clinic attendance during and after treatment or while under observation for venereal disease at the Royal Infirmary, Edinburgh, or the General Infirmary, Leeds, during 1948–9 of four groups of male patients: (1) 161 with early (primary and secondary) syphilis; (2) 24 with early latent syphilis; (3) 421 patients exposed to the risk of venereal disease and advised to remain under orthodox observation; and (4) 502 who were advised to remain under observation following treatment for gonorrhoea. Treatment schedules are described; these varied within narrow limits but all patients with syphilis received penicillin, arsenic, and bismuth. The term "defaulter" is defined and the pattern and rate of default are analysed.

In the first group 4 out of 161 patients did not complete the penicillin course, and another 25 failed to complete the first unit course of arsenic and bismuth (default rate 17%); 70 were recommended a second unit course, but 4 of these failed to return after the rest period and 7 defaulted before the end of the second course (default rate 16%). The total default rate up to the end of treatment (40 in 161) was 25%. Fifteen patients were persuaded to return, but all soon defaulted again and it was concluded that patients "would either complete their treatment or would not, irrespective of any steps taken to influence them". The default rate was not related to the stage of disease, history of previous venereal infection, or to whether treatment was entirely on an out-patient basis or included initial admission to hospital. There was no significant difference in the rates for single and married men, but in the small group of men divorced or separated from their wives the default rate was significantly high (7 out of 16, or 44%). Maximum default occurred in the 20 to 24 age group and decreased

with increasing age, but the few patients under the age of 20 did not default. The material did not lend itself to satisfactory analysis from the standpoint of occupation, but within its limitations it showed a lower default rate amongst those whose work called for perseverance and reasonable standards of intellect, such as miners, as compared with those in less exacting occupations, such as labourers and drivers. The small " white-collar " group had a high default rate.

The pattern of default in the other groups was identical with that of the group treated for early syphilis, while the pattern amongst patients treated in Edinburgh was paralleled by that of the Leeds cases. This study supports the current emphasis on " case-finding " rather than " case-holding ", but the author condemns an attitude of cynical pessimism and calls for the preservation of an idealistic approach and the maintenance of the highest professional and ethical standards.

S. M. Laird

307. **The Diagnosis and Test of Cure of Chronic Prostatitis.** (Zur Diagnose und Feststellung der Heilung der chronischen Prostatitis)

G. RIEDEL. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **10**, 25–34, 1951. 27 refs.

Results of diagnostic tests for chronic prostatitis, such as palpation, expression, and the two-glass test, may be negative; phosphaturia, prostatorrhoea, and disturbance of micturition may be absent in spite of the presence of infection; this condition is called dry prostatitis by some authors. To diagnose the presence or absence (that is, cure) of chronic prostatitis and to differentiate it from sexual neurasthenia a new method of investigation is described.

The report is based on 43 cases from the dermatological clinic of the University of Tübingen. From none of these cases were gonococci cultured; 17 patients gave a history of gonorrhoea; 6 of these had a positive gonococcal complement-fixation reaction, but 3 only after a provocative dose of streptomycin. In the method described use is made of all the above-mentioned tests, but in addition total and differential leucocyte counts are performed and the erythrocyte sedimentation rate (E.S.R.) measured 1, 2, and 24 hours after prostatic massage. This is of course contraindicated in acute cases.

A variation of at least 800 per c.mm. in the count of polymorphonuclear leucocytes is regarded as diagnostic. The author has not found a lymphocytosis, monocytosis, and shift to the right as previously described, but a shift to the right and fall in lymphocyte count. The E.S.R. rose in all cases of haematogenous chronic prostatitis, but in only 26% of the post-gonorrhoeal cases and in 23% of the non-specific cases. The changes in the total and polymorphonuclear leucocyte counts were found in 90% of all cases, though in some cases only one of the two gave significant results.

As prostatic massage may produce a fall in blood pressure, the latter was determined at 1, 3, and 10 minutes after prostatic massage; in one case in the series the pressure fell from 145/95 to 110/75 mm. Hg.

Ferdinand Hillman

SYPHILIS

308. **Treatment of Syphilis with Penicillin : Review of 123 Cases Treated in H.M. Forces**

R. LEES and L. WATT. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **26**, 174–176, Dec., 1950. 3 refs.

Many cases of early syphilis occurring in members of the armed forces in 1945 and 1946 were treated with penicillin alone. The dosage then in general use was 2·4 mega units (40,000 units 3-hourly for 7½ days), which is now recognized as being below the optimum. These men have now returned to civilian life and, although many have failed to undergo the clinical and serological surveillance recommended on their release, some have, for different reasons, been re-examined. The authors here report their findings in 123 such cases, in 89 of which the period of observation was 24 months or longer. Brief case records are given of 7 of these patients in whom relapse or re-infection was observed. Two of them had infected their wives after completing treatment, and had presumably themselves suffered an infectious clinical relapse; one was found to have early asymptomatic meningeal syphilis. Two other patients suffered clinical relapse 4 months and 6 months respectively after treatment, but in the remaining 3 cases reinfection may have occurred. All cases responded satisfactorily to retreatment with penicillin supplemented with arsenic and bismuth.

S. M. Laird

309. **Therapeutic Paradox from Penicillin Therapy in Laryngeal Syphilis. Report of a Case**

A. I. SUCHETT-KAYE. *British Journal of Venereal Diseases* [*Brit. J. vener. Dis.*] **26**, 183–184, Dec., 1950. 1 ref.

A male patient, aged 34, complained of general malaise, sore mouth and throat, dysphagia, and rectal discharge of 3 weeks' duration. Examination revealed a toxic, ill patient with anal condylomata lata, recently healed preputial chancre, and a slightly husky voice. Fauces and palate showed confluent, greyish " mucous patches ", and cervical adenitis was well marked. *Treponema pallidum* was readily demonstrated in scrapings from the anal condylomata and the Wassermann and Kahn reactions were both positive.

The patient was given a total of 8 mega units of penicillin intramuscularly in 3-hourly doses of 100,000 units, and 6 days after starting penicillin therapy the first of 10 weekly injections of bismuth was given. A typical Herxheimer reaction, with rigor and temperature up to 102·4° F. (39·1° C.), developed 8 hours after the first dose of penicillin, and clinical recovery proceeded rapidly. From the 11th day, increased hoarseness of the patient's voice was noted which became so severe that, on the 21st day, a laryngologist was consulted; the epiglottis and vocal cords showed infiltration, fibrosis, and slight deformity, but the airway was not obstructed. On the 36th day, well-advanced epiglottic scarring was noted, but the airway still remained free and the hoarseness was much less marked. Some 4 months after the

start of treatment the voice had returned to normal. The author regards the laryngeal symptoms and signs as an example of " therapeutic paradox " due to the very rapid resolution of the syphilitic lesions in the larynx.

S. M. Laird

310. **Results of Penicillin Therapy for Neurosyphilis at Bellevue Hospital**

B. DATTNER, E. W. THOMAS, and L. DE MELLO. *Journal of Venereal Disease Information* [*J. vener. Dis. Inform.*] **32**, 33–39, Feb., 1951. 3 refs.

Over 600 patients with neurosyphilis have now been treated with penicillin alone at Bellevue Hospital, New York. Of these 555 had active neurosyphilis with a raised cell count in the cerebrospinal fluid, and 438 of these were subjected to further cerebrospinal-fluid examinations 6 months or more after treatment. A few patients were transferred to mental hospitals and 15 are known to have died, although none of the 15 deaths was attributable directly to syphilis.

Of the 438 patients, 114 had asymptomatic neurosyphilis, 90 meningovascular syphilis, 82 tabes dorsalis, 67 general paresis, 31 tabo-paresis, 40 optic atrophy, and 14 Erb's spastic paralysis. The dose of penicillin (in millions of units) was as follows: 29 patients, 2; 38 patients, 3; 70 patients, 4; 42 patients, 5; 205 patients, 6; 4 patients, 7·2; and 50 patients, 9.

During a follow-up of 6 to 75 months the fluid of 400 became inactive. Of the 38 failures only 31 were retreated at Bellevue: 25 were retreated only once, 3 twice, and 3 three times. Of the 31 retreated patients, 27 had inactive fluid when last examined, 2 were not followed up for 6 months after treatment, and 2 failed to respond. The authors recommend procaine penicillin with 2% aluminium monostearate, giving 15 daily injections of 600,000 units each.

R. R. Willcox

311. **The Combined Treatment of Recent Syphilis with Arsphenamine and Penicillin.** (Über kombinierte Salvarsan–Penicillin-Behandlung der rezenten Lues)

H. T. SCHREUS and W. GAHLEN. *Dermatologische Wochenschrift* [*Derm. Wschr.*] **10**, 34–41, 1951. 1 fig., 14 refs.

Of recent syphilitic infections 80% can be considered to be cured by arsphenamine treatment; a similar proportion would respond to penicillin therapy. The authors consider that the 20% residue of resistant cases in the two groups need not be identical and have therefore combined the penicillin and arsenical treatments. They gave 6,000,000 units of penicillin in 16 days, giving one injection of 400,000 units daily, together with a simultaneous course of neoarsphenamine and bismuth, the latter lasting 20 days longer than the penicillin course. The progress of each case was assessed periodically, serum reactions being marked as + to ++++ and the following tests used: the Wassermann reaction with an extract of beef heart, the Wassermann reaction with syphilitic liver, the Wassermann–Schreus reaction, the citochol reaction, the Meinicke clearing reaction, and the Sachs-Georgi reaction. All these tests were carried out in each assessment; the results were added up and divided by two. The results showed that up to a reading of 5 only flocculation reactions were positive and between 7 and 12 the complement-fixation reactions became positive. By this method a parallelism between clinical findings and complement-fixation reactions appears. A diagram which illustrates the results in 22 cases is reproduced.

At the end of the first course of treatment 12 cases were Wassermann-negative; 5 weeks later, without any additional treatment, a further 8 were negative. During the same interval the strength of flocculation reactions in the first-mentioned 12 cases had decreased and reactions had become negative in 3 cases. The serological reactions therefore changed more rapidly than after penicillin treatment and more regularly than after arsenic and bismuth therapy.

The authors intend to cut down the doses employed at present and to determine a " minimum effective dose " in order to reduce the duration of administration and thus develop a " short cure ". At present they are treating a series of cases with the 16-day course of penicillin as above, but with the arsphenamine–bismuth part of the course limited to the 16 days during which penicillin is given and the total dose of neoarsphenamine and bismuth reduced.

Ferdinand Hillman

312. **Njovera: an Endemic Syphilis of Southern Rhodesia. Comparison with Bejel**

R. R. WILLCOX. *Lancet* [*Lancet*] **1**, 558–561, March 10, 1951. 1 fig., 12 refs.

Among the natives of some rural areas of Southern Rhodesia there occurs an endemic disease which closely resembles syphilis and is known as " njovera ". The disease does not appear to be of venereal origin and is usually first seen in children. Njovera is not generally recognized until the stage of generalization occurs, the lesions of which (mucous patches on the lips, vulval and anal condylomata, adenitis, and framboesiform cutaneous lesions) follow the general pattern of the secondary stage of syphilis. Although the primary lesion is rarely identified, the author considers that the transmission of the infection is non-venereal: he places the responsibility for the dissemination of the infection upon such factors as dirt, overcrowding, flies, and communal feeding habits and implements.

The Kahn test is usually positive, and from the moist lesions an organism indistinguishable from *Treponema pallidum* is readily obtained. The lesions heal rapidly after treatment with penicillin, bismuth, or neoarsphenamine. The incidence of the disease appears to be diminishing and this decline is ascribed to the effects of anti-syphilitic treatment, facilities for which are available in government clinics. Points of similarity to, and diversity from, syphilis and bejel are discussed. The author believes that njovera and bejel are in fact syphilis.

V. E. Lloyd

See also Section Hygiene and Public Health, Abstract No. 3.

Genito-urinary Disorders

313. **Nephrocalcinosis**
W. J. ENGEL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **145**, 288–294, Feb. 3, 1951. 5 figs., 8 refs.

The author describes 7 cases of diffuse calcification of both kidneys. The calcification usually appears in the pyramids and can easily be seen on *x*-ray examination. There is evidence that calcification is the result of tubular damage, and in some cases this damage is the direct result of a toxic action of sulphonamides. In 6 of the 7 cases reported sulphonamides had been given. The treatment suggested is a low-salt diet, a citrate mixture, vitamin B in normal doses, and a diet containing an adequate amount of calcium. *Victor W. Dix*

314. **The Effect of Antihistaminics on the Evolution of Experimental Glomerulonephritis.** (Accion de los antihistaminicos en la evolucion de la glomerulo-nefritis experimental)
E. ACEVEDO and J. SAFIAN. *Revista Médica de Chile* [*Rev. méd. Chile*] **78**, 707–709, Nov., 1950. 11 refs.

Acute nephritis was induced in 7 rabbits with Masugi nephrotoxic serum; 6 of the animals were given intraperitoneal injections of "antistin" (2-(N-phenyl-*n*-benzylaminoethyl)-iminazoline) 96 hours later, and daily for the next week. The dose was 5 mg. per kg. body weight. The control animal developed a severe nephritis, but did not die. Two of the 6 treated animals died and 4 survived. These had intermittent albuminuria, and renal biopsy showed that 2 had scattered lesions involving both glomeruli and tubules, while the other 2 appeared normal histologically. The control animal showed diffuse and severe glomerular and tubular damage which the authors have previously demonstrated to be the rule. They conclude that antistin given 96 hours after the induction of experimental nephritis has a curative effect. When given sooner it is even more effective. *K. Gurling*

315. **Acute Glomerulonephritis Treated with Antihistaminics.** (Glomerulonefritis aguda tratada con antihistaminicos)
O. HERRERA, C. J. BARROS, and B. RODRIGUEZ. *Revista Médica de Chile* [*Rev. méd. Chile*] **78**, 710–715, Nov., 1950. 2 figs., 14 refs.

A group of 27 patients with acute nephritis were treated by routine methods together with parenteral "antistin" (2-(N-phenyl-*n*-benzylaminoethyl)-iminazoline). A control group of 58 similar patients treated in previous years by the usual methods was used for comparison. It is claimed that the blood pressure returned to normal more rapidly in the antistin-treated group, that the oedema disappeared more rapidly, and that the urine returned to normal in 96% of cases as opposed to 62% in the control group. The duration of stay in hospital was not reduced, possibly because tonsillectomy was performed in 33% of the treated group as against 7 to 8% in the others. It is concluded that antistin exerts a curative effect in acute nephritis.

[More details concerning the blood pressure and urinary changes would be enlightening.]

K. Gurling

316. **Treatment of Nephrosis with Cortisone**
J. A. LEUTSCHER and Q. B. DEMING. *Journal of Clinical Investigation* [*J. clin. Invest.*] **31**, 1576–1587, Dec., 1950. 5 figs., 21 refs.

In a study of the effect of cortisone on the various manifestations of the nephrotic syndrome in 11 patients at Stanford University School of Medicine, San Francisco, the sodium-retaining activity of the urinary corticoids, which is increased in the nephrotic syndrome, was measured by biopsy in adrenalectomized rats by comparison with the effect of a standard dose of deoxycortone acetate. As might be expected, during cortisone administration (100 to 300 mg. a day for 5 to 16 days) some manifestations of the renal upset were made worse. Albuminuria and oedema tended to increase, sodium excretion diminished, and the serum protein level rose a little. In 2 cases a rise in serum potassium level prevented the completion of treatment. When cortisone was stopped, however, diuresis occurred in 6 patients with loss of all oedema for periods which ranged from a few days to several months, usually starting 3 days after cortisone was stopped. There was also a reduction in the albuminuria and excretion of sodium-retaining corticoids. Creatinine excretion increased, as did the serum sodium level. There was no alteration in serum cholesterol level, haematocrit, or erythrocyte sedimentation rate. [The blood urea level is not mentioned.] The value of cortisone is thus apparent only after its withdrawal, during the time when endogenous adrenal activity is depressed. Experimentally, adrenalectomy will reduce albuminuria, and intercurrent infection is known to bring about clinical improvement in cases of wet nephritis. The other 5 patients were not improved, but the subsequent improvement of 4 of them following intravenous albumin therapy is reported, and these two forms of treatment may be complementary. The authors point out that the fundamental disorder in this disease still appears to lie in the kidney. *K. Gurling*

317. **Chronic Renal Disease with Secondary Hyperparathyroidism**
D. G. B. RICHARDS. *British Medical Journal* [*Brit. med. J.*] **1**, 167–169, Jan. 27, 1951. 13 refs.

The author, after reviewing the literature on the subject, describes a fatal case of nephritis with gross enlargement of the parathyroid glands in a woman aged 44 years, who had bone changes of osteitis fibrosa and widespread

arterial calcification. The functional relationship between chronic renal disease and the parathyroid gland is discussed. Phosphorus is not excreted by the diseased kidneys and its retention in the blood causes a fall in serum calcium concentration, which in turn stimulates the parathyroid gland, causing hyperplasia and an increase in production of the hormone, which mobilizes calcium from the bones; the serum calcium level is thus raised to normal or higher from the earlier low level. Over-saturation of the blood and tissues with calcium phosphate may lead to the precipitation of calcium salts in the tissues with widespread calcification, as shown in the author's case. *S. Karani*

318. **Sodium and Potassium Excretion in Chronic Renal Failure**
R. PLATT. *Clinical Science* [*Clin. Sci.*] **9**, 367–377, Nov. 30, 1950. 3 figs., 10 refs.

The renal mechanisms which enable many patients with chronic renal failure to preserve normal plasma levels of sodium and potassium were investigated in the Department of Medicine of the University of Manchester by the comparison, in 26 cases of renal failure, of sodium and potassium clearances with those of inulin or endogenous creatinine. It was found that in patients with renal failure a smaller proportion of the filtered load of sodium was reabsorbed in the tubules, so that the total excretion of sodium was maintained in spite of gross reduction in filtration rate. In the case of potassium, not only was reabsorption by the tubules depressed, but in some patients potassium clearance exceeded considerably both inulin and creatinine clearance. The most likely explanation is that the tubules excrete potassium in these patients. *D. A. K. Black*

319. **Intestinal Perfusion in the Treatment of Acute Renal Insufficiency.** (La perfusion intestinale dans le traitement de l'insuffisance rénale aiguë)
J. HAMBURGER, G. MATHÉ, and J. CROSNIER. *Bulletins et Mémoires de la Société Médicale des Hôpitaux de Paris* [*Bull. Soc. méd. Hôp. Paris*] **66**, 1716–1727, Dec. 8, 1950. 2 figs., 8 refs.

320. **Renal Function Studies in Acute Tubular Necrosis**
G. M. BULL, A. M. JOEKES, and K. G. LOWE. *Clinical Science* [*Clin. Sci.*] **9**, 379–404, Nov. 30, 1950. 16 figs., 30 refs.

The clinical course of 33 cases of anuria or severe oliguria from various causes was studied, and renal function investigated by the application of clearance techniques and the determination of extraction ratios in renal venous as compared with arterial blood. Four phases could be differentiated: (1) Onset. (2) Anuric or oliguric phase, in which renal blood flow and glomerular filtration rate (G.F.R.) were greatly reduced and the presence of gross tubular damage was shown by inability to concentrate urea and creatinine, to conserve electrolytes, or to extract *p*-aminohippurate normally. (3) Early diuretic, in which the daily urine volume exceeded one litre, but there was still evidence of gross reduction in renal blood flow, G.F.R., and tubular efficiency. (4) Late diuretic, in which the renal blood flow and G.F.R. approached normal, but might not reach normal values even after long observation.

The association of a low renal blood flow in the oliguric phase with a high arterio-venous oxygen difference excludes the participation of an intrarenal shunt of any magnitude. The therapeutic implications of these findings are discussed.

[This paper merits study in full.] *D. A. K. Black*

321. **Intermittent Peritoneal Lavage in Nephrectomized Dogs and its Application to the Human Being**
A. GROLLMAN, L. B. TURNER, and J. A. MCLEAN. *Archives of Internal Medicine* [*Arch. intern. Med.*] **87**, 379–390, March, 1951. 3 figs., 23 refs.

Dogs were kept alive after nephrectomy for periods varying between 30 and 70 days by means of intermittent peritoneal lavage repeated twice daily, the technique of which is described. A 17-gauge needle, 9 cm. long, is inserted into the flank of the animal and one litre of a hypertonic irrigating fluid introduced into the peritoneal cavity, left for a varying time, then drained off (this takes 30 minutes), the cavity re-filled (this takes 5 minutes), and the needle withdrawn until the procedure is repeated the next time. Osmotic pressure between plasma and fluid in the peritoneal cavity is at equilibrium after about 2 hours, the exchange of fluid depending mainly on the concentration of glucose in the rinsing fluid. When this is 2% or more, for 2 to 6 hours after the filling procedure, excess glucose disappears from the peritoneal cavity and fluid passes from the tissues into it (averaging 86 ml. per litre of fluid containing 3% glucose). Later on, when the glucose level has been reduced, the flow is reversed. With 3% of glucose in the peritoneal fluid, urea passes into it within the first hour up to a concentration of 200 mg. per 100 ml., with only a small further rise in the following 6 to 8 hours. The electrolyte concentrations in the perfusion fluid used by the authors, in mg. per l., were as follows: NaCl, 5·77; $CaCl_2$, 0·2; $MgCl_2$, 0·05; KCl, 0·2; $NaHCO_3$, 3·0. The dogs were fed through a tube on a synthetic food containing 2,230 Calories per litre, 70 Calories being given per kg. body weight. To overcome the anaemia inevitably occurring in uraemia the dogs had to be given a blood transfusion about once every 10 days.

In 5 patients with anuria who were subjected to intermittent peritoneal lavage striking results were obtained: in 3 cases consciousness returned, pulmonary oedema disappeared, and the blood urea concentration was reduced to a considerable, though varying, degree. The procedure described was modified in a that polythene tube was inserted in the midline below the umbilicus, and 25,000 units of penicillin and 25 mg. of streptomycin were added to each litre of perfusion fluid and 300,000 units of aqueous procaine penicillin were given daily by injection. No heparin was used. *L. H. Worth*

322. **Variability of the Sperm Count**
G. C. KENNEDY, N. A. RICHARDS, and P. M. F. BISHOP. *British Medical Journal* [*Brit. med. J.*] **1**, 559–560, March 17, 1951. 1 ref.

Disorders of the Locomotor and Osseous Systems

323. **Effect of Cortisone and Pituitary Adrenocorticotropic Hormone (ACTH) on Rheumatic Diseases**
P. S. HENCH, C. H. SLOCUMB, H. F. POLLEY, and E. C. KENDALL. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **144**, 1327–1335, Dec. 16, 1950. 1 fig., 37 refs.

The anti-rheumatic properties of cortisone and pituitary adrenocorticotrophic hormone (ACTH) have been confirmed by several groups of investigators.

During the time of their administration, these hormones have exerted a decidedly suppressive effect on the clinical and biochemical manifestations of rheumatoid arthritis. When the use of the hormones is discontinued symptoms recur rather promptly in most cases, but in several of our cases pronounced improvement has persisted for several (7 to 14) months. The optimal dosage and methods of administration of these hormones for the investigative management of a chronic disease such as rheumatoid arthritis remain to be determined. Several schemes are under investigation. Rather prolonged relief with minimal side effects has been provided in some cases by the continued use of small maintenance doses after the earlier use of larger suppressive doses.

Cortisone or pituitary adrenocorticotrophic hormone generally abolishes quickly the manifestations of acute rheumatic fever. There is reason to believe that the lesions of acute rheumatic carditis also are suppressed, in consequence of which the prevention of certain chronic cardiac lesions may be anticipated with some confidence, especially if adequate hormonal usage during the acute rheumatic state is followed by prolonged chemoprophylaxis (for example, with penicillin given orally). The articular complications of disseminated lupus erythematosus and psoriasis are responsive to these hormones. Limited results were obtained in 2 cases of tuberculous arthritis.

These hormones are powerful agents which may affect many functions and tissues of the body besides those of joints and muscles. Their prolonged use, at least in certain doses, may produce certain undesirable effects. These side effects have, to date, been transient and reversible. Certain measures have been developed to minimize or control some of them, but these effects still constitute an important problem for further investigation. If control of the side effects is not adequate in any given case, smaller doses of the hormones should be used and patient and physician alike should be content with a reduced amount of symptomatic relief.

With the exception of 17-hydroxycorticosterone (compound F of Kendall), none of the currently available steroids chemically related to cortisone appears to have significant anti-rheumatic properties. The oral administration of one specially prepared extract of adrenal cortex containing compounds E (cortisone) and F produced appreciable relief in one case of rheumatoid arthritis and has lent support to the belief that cortisone, and perhaps also compound F, will be chemically effective when given orally.

The mode of action of cortisone and pituitary adrenocorticotrophic hormone in rheumatic diseases is not yet known, but the hormones appear to provide to the tissues affected in these diseases a shield-like buffer against a variety of irritants.

The results of recent and current investigative studies appear to provide justification for the impending restricted application of these hormones to the field of therapy, at least in certain acute rheumatic and articular conditions. —[Authors' summary.]

324. **Combined Administration of Desoxycorticosterone Acetate and Ascorbic Acid. I. Clinical Results in Rheumatoid Arthritis and Laboratory Studies**
J. B. R. MCKENDRY, C. A. SCHAFFENBURG, and E. P. MCCULLAGH. *Archives of Internal Medicine* [*Arch. intern. Med.*] **87**, 190–198, Feb., 1951. 35 refs.

Combined treatment was given to 23 patients suffering from rheumatoid arthritis. There were no controls. Of the 16 patients who received more than two treatments 9 reported definite improvement within a few days. *D. P. Nicholson*

325. **Combined Administration of Desoxycorticosterone Acetate and Ascorbic Acid. II. Experimental Observations**
C. A. SCHAFFENBURG, J. B. R. MCKENDRY, and E. P. MCCULLAGH. *Archives of Internal Medicine* [*Arch. intern. Med.*] **87**, 199–203, Feb., 1951. 26 refs.

The effects of the combined administration of deoxycortone acetate and ascorbic acid to mice were studied by means of the cold test, egg-white reaction, and formaldehyde-induced arthritis. It is concluded from the results of these experiments that this combined administration has no cortisone-like activity. It showed no protective effect in mice against formaldehyde-induced arthritis, in contrast to the previously reported work of Brownlee. *D. P. Nicholson*

326. **Plasmacytosis in the Bone Marrow in Rheumatoid Arthritis**
F. G. H. HAYHOE and D. R. SMITH. *Journal of Clinical Pathology* [*J. clin. Path.*] **4**, 47–54, Feb., 1951. 5 figs., 18 refs.

The possibility of a connexion between plasma cells, antibody formation, and hyperglobulinaemia was studied in the Department of Medicine, Cambridge University. In 10 consecutive cases of rheumatoid arthritis of variable duration and severity bone marrow was examined, plasma protein levels were estimated by a micro-Kjeldahl technique, and the erythrocyte sedimentation rate was measured. The plasma-cell elements of the

marrow were classified as plasmablasts, proplasmacytes, plasmacytes, plasmacytes showing early homogeneous degeneration, and degenerative plasmacytes. The proportion of all plasma cells in the preparations was 1·8 to 6·3 per 100 marrow cells. A finding of more than 2% is certainly abnormal, but even figures higher than 3%, the presence of nuclear and cytoplasmic abnormalities in plasma cells, and the finding of multinucleated cells are not absolutely diagnostic of multiple myelomatosis without supporting evidence. A definite increase in the plasma globulin level was noted in every case. It is suggested that the hyperglobulinaemia of rheumatoid arthritis is an antibody response, accompanied by plasmacytosis, to an unknown antigen.

[These findings agree substantially with those of Leitner, Britton, and Neumark (*Bone Marrow Biopsy*, London, 1949). It is probable that plasma cells are concerned with the production of globulins.]

E. Neumark

327. **Pregnenolone in Rheumatoid Arthritis**

J. R. DORDICK, M. E. ERHLICH, S. ALEXANDER, and M. KISSIN. *New England Journal of Medicine* [*New Engl. J. Med.*] **244**, 324–326, March 1, 1951. 10 refs.

Twenty-five patients with rheumatoid arthritis and 8 patients with other diseases were given pregnenolone, either orally or intramuscularly, or by both routes. Dosage varied from 300 to 1,000 mg. daily. Patients were observed for an average of 14 weeks. Two patients with rheumatoid arthritis improved; 4 had slight, questionable improvement, but in all others no significant benefits were obtained. Two patients developed headache, which disappeared with reduction of dosage. After the use of intramuscular administration, painful local induration occurred regularly; sterile abscesses formed, requiring drainage, in 2 cases.—[Authors' summary.]

328. **Therapeutic Suppression of Tissue Reactivity. II. Effect of Aminopterin in Rheumatoid Arthritis and Psoriasis**

R. GUBNER, S. AUGUST, and V. GINSBERG. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **221**, 176–182, Feb., 1951. 1 fig., 24 refs.

The scarcity of cortisone and ACTH, together with the reports of untoward side-effects following their prolonged administration, has stimulated investigation of a large number of steroids which might be thought to have somewhat similar properties. On the assumption that the beneficial effect of cortisone in arthritis may lie in the power of inhibiting connective-tissue proliferation, the authors have used the folic acid antagonist 4-aminopteroylglutamic acid (aminopterin) in the treatment of 7 cases of rheumatoid arthritis and one of rheumatic fever. The daily dosage employed was 1 to 2 mg., the total ranging from a minimum of 6 mg. to 40 mg. over periods varying from 6 to 21 days. It was found that although aminopterin has no analgesic effect it produced significant clinical amelioration in 7 of the 8 cases treated. There was no evidence, however, of any effect upon the course of the disease as indicated by the erythrocyte sedimentation rate, serum protein level, or leucocyte changes. As is often the case also with cortisone therapy, withdrawal symptoms in the form of acute exacerbation of the arthritic process for several weeks occurred.

It was not thought that the clinical effect of aminopterin is mediated through the pituitary or adrenal routes, but that it is due to direct inhibition of mesenchyme and, to a lesser extent, epithelial tissues. The toxic effects of aminopterin unfortunately appear to place a limitation on its practical use as a therapeutic agent.

W. S. C. Copeman

329. **Felty's Syndrome. A Report of Four Cases Treated by Splenectomy**

M. S. R. HUTT, J. S. RICHARDSON, and J. S. STAFFURTH. *Quarterly Journal of Medicine* [*Quart. J. Med.*] **20**, 57–73, Jan., 1951. Bibliography.

Felty's syndrome is defined as a triad of rheumatoid arthritis, splenomegaly, and neutropenia. This association of signs had been noted by many workers long before Felty (1924) recognized it as a clinical entity and gave a description of 5 cases in middle-aged men and women. This paper deals with 4 cases, 1 in a man and 3 in women. Splenectomy was performed in all of them with good results. The most striking feature was the improvement in general health, which was found to be maintained a year later. Eye complications such as corneal ulcer and hypopyon tended to clear up; ulcers in the mouth and on the legs healed well. The leucocyte count was restored to normal, which is held responsible for most of the improvement. The arthritis also improved. Some of the features of the syndrome are ascribed to hypersplenism, whose *modus operandi* is discussed. The authors urge the use of splenectomy in Felty's syndrome, unless there are definite contraindications.

D. Preiskel

330. **The Manubrio-sternal Joint in Ankylosing Spondylitis**

D. L. SAVILL. *Journal of Bone and Joint Surgery* [*J. Bone Jt Surg.*] **33B**, 56–64, Feb., 1951. 14 figs., 13 refs.

The radiological appearances of the manubrio-sternal joint in a series of 61 cases of ankylosing spondylitis are described, comparison being made with a similar group of healthy persons and a smaller group of patients with polyarticular rheumatoid arthritis. Narrowing and eventual fusion of the joint were found in a high proportion of the patients with spondylitis, all those over 35 years of age showing this feature. The changes in the manubrio-sternal joint are regarded as similar to those found in the sacro-iliac joint.

The superficial location of the manubrio-sternal joint made it possible to undertake biopsy examination in 5 cases, including one in which the joint was fused. The cartilage was found to be replaced by fibrous tissue which involved the adjacent bone ends, but which did not show any inflammatory reaction.

H. A. Sissons

See also Sections Pathology, Abstract 143; Disorders of the Blood, Abstract 245.

Neurology

331. **The Effect of Head Posture on the Manometrics of the Cerebrospinal Fluid in Cervical Lesions: a New Diagnostic Test**
L. KAPLAN and F. KENNEDY. *Brain* [*Brain*] **73**, 337–345, 1950. 4 refs.

The authors have noted that in certain cases Queckenstedt's test gives results which are difficult to understand. In one group of cases there is an absence of manometric block in patients with surgically-confirmed compressing lesions, and in another the presence of what appears to be a complete manometric block is associated with a consistently normal spinal-fluid protein content.

A variation in the technique of the test was therefore instituted. After inserting the needle in the ordinary position, jugular compression was performed first with the head in the usual position—in line with the trunk; secondly with the head fully flexed; and thirdly with the head fully extended. It is essential that the puncture be performed in the midline and that abdominal compression be carried out after each change of posture, so as to be sure that the needle is still properly *in situ*. They recommend manual jugular compression rather than compression by an inflated cuff, and warn that neck manipulations are dangerous in recent acute cervical spine injury and in lesions of the foramen magnum.

Among their cases were 31 with clinical diagnoses of cord-compressing lesions in the cervical region; 3 showed complete block unchanged by variations in head posture, in 16 all results were normal, and in 12 the result was abnormal in one of the 3 positions—10 in extension, 2 in flexion. Of these 12 patients 8 were explored; in 4 cases exotoses were found, in 2 a prolapsed disk, and in the other 2 adhesive arachnoiditis of the middle and lower cervical regions. The authors consider that the site of the lesions provides a mechanical explanation for the production of the block by placing the head in extension. In 4 cases they were able to confirm the intermittent block radiographically, holding up the oil by hyperextending the head and then allowing it to flow down by flexing the head.

The test would appear to be quite specific, as none of their control cases showed this intermittent block.

N. S. Alcock

332. **Internal Muscular Pressure and Muscle Tone in Neurological Diseases.** (Muskelinnendruck und Muskeltonus bei neurologischen Erkrankungen)
G. HEUCHEL and R. ZIPPEL. *Klinische Wochenschrift* [*Klin. Wschr.*] **29**, 178–180, March 1, 1951. 7 refs.

With the method developed by Henderson and the apparatus used by Beiglboeck and Funk the internal pressure of skeletal muscles was examined in healthy persons and more particularly in those suffering from pathological disorders of the muscle tone. Since, in the opinion of Henderson, the internal pressure of a muscle is a measurable expression of its tone, its investigation in neuromuscular disorders is of particular interest. In conformity with other workers the average pressure in healthy muscles was found to be about 76 mm. H_2O, being the same in most of the muscles of both limbs and fairly constant in the same person. No essential differences were found between males and females. The pathological cases, however, brought forth some unexpected results. In neuromuscular disorders of peripheral or spinal origin with clinical signs of hypotonic paresis or wasting the internal pressure of the involved muscles was markedly reduced when compared with the corresponding healthy ones, thus showing in fact a parallelism between the pressure and the tone which was not, however, found in hypertonic muscles. In a case of hemiplegia with pronounced spasticity and other signs of increased muscle tone the internal pressure of the spastic gastrocnemius was less than one-half of that on the normal side. Similar results were found in cases of spastic paraplegia, disseminated sclerosis, and Parkinsonism.

It is evident that in muscle disorders of peripheral or central origin the internal pressure is always reduced, regardless of the clinical condition of the involved muscles, which may be in a state of increased or decreased tone. It must thus be concluded that the estimation of internal muscle pressure cannot be used as a measurement of the tone condition in a given muscle.

F. F. Kino

333. **Electrical Activity of the Human Brain during Artificial Sleep. I. The Cyclical Pattern of Response to Barbiturate Sedation**
B. D. WYKE. *Journal of Neurology, Neurosurgery and Psychiatry* [*J. Neurol. Neurosurg. Psychiat.*] **13**, 288–295, Nov., 1950. 7 figs., 16 refs.

This paper is concerned with the cyclical changes induced by "seconal sodium" (sodium 5-allyl-5-(1-methylbutyl) barbiturate) in the human electroencephalogram (EEG). Observations were made on 5 normal adults while they were put to sleep with graduated doses of this drug given orally, the total amount administered not exceeding 4·5 gr. (0·3 g.). EEG tracings were made at frequent intervals from all areas of the head, and attempts were made to correlate the EEG changes with depth of sleep by examining the subject at various stages.

The sequence of cerebral electrical changes was found to parallel closely that originally described by Loomis *et al.* in 1937. Furthermore, although the narcotized subjects in this examination seldom passed into the deepest stages of sleep, they passed through the stages characteristic of normal sleep, and the correlation between depth of sleep and EEG changes was similar to that obtaining in normal sleep.

Chronologically, the similarity of the changes occurring in normal and in seconal-induced sleep is sufficiently close to suggest the operation of a similar

mechanism in the two cases. The material here discussed is considered to favour the possibility that the barbiturate exerts a specific central action; evidence bearing on this point is to be presented in a subsequent communication. *Maurice Parsonage*

334. **The Electroencephalogram of the Premature Infant.** (Über das Elektrencephalogram von Frühgeburten)
H. Mai, E. Schütz, and H. W. Müller. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **69**, 251–261, 1951. 7 figs., 15 refs.

Prognosis as to the survival of a premature infant depends largely on its stage of maturity, this being best judged by the body weight. The brain, constituting 15% or more of the total body weight in such infants, is particularly exposed to injury at the time of birth, but the high mortality is due in considerable part to the defective function of the centres regulating temperature, respiration, and food intake. Immaturity of the important centres, if the baby survives, is not of long duration, whereas the consequences of traumatic lesions such as intracranial haemorrhages may appear in later years, causing epilepsy or defective intelligence. The early diagnosis of any such lesions is therefore of paramount importance, but for obvious reasons is difficult to carry out.

In order to explore the possibility of using the electroencephalograph (EEG) as a diagnostic help in the detection of cerebral lesions in premature infants the authors developed a method of recording active currents in such cases. They found in 14 cases that, as in normal infants, short bursts of rhythmic waves varying continuously in frequency and localization were superimposed occasionally on a constant arrhythmic pattern. Records made during sleep showed bursts of much longer duration, differing characteristically, however, from the rhythms observed in sleeping adults in that they were dysrhythmic rather than arrhythmic, that is, discharges occurred at several frequencies alternating rapidly, it being noted that the slow waves were markedly fewer than those at 8 to 10 and at 20 c.p.s. The curves in fact resembled those obtained from the sub-cortex in animal tests (cats, rabbits) by means of a Hess electrode. From this the authors are led to conclude that the bursts of long duration seen in the sleeping EEG are of sub-cortical origin, and that the shorter bursts seen during waking presumably originate from the cortex.

In normal infants the cortical rhythm becomes "consolidated" at about 6 weeks after birth, that is, it is limited to the region of the central gyri and its frequency stabilized at about 15 c.p.s. In the premature infant, however, this rhythm may be very weak in the central area at 6 weeks, or may become noticeable only at a later stage. Its appearance generally coincides with the appearance of signs of independence in the infant, such as spontaneous sucking.

In normal infants the α-rhythm is present at the age of 4 months and is also detectable occipitally. In the mentally defective it is not present until much later. In premature infants, however, the authors found that the α-rhythm appeared at the same interval after birth, although it was not so marked, as in normal infants. In both normal and premature infants the amplitude of the slow wave is greater during sleep, increasing from 50 microvolts to 100 or 120 microvolts. Similar results have been observed in the EEG of tired adults from whom, when aroused by sudden noise or bright light, the more rapid α-waves were recorded instead of the usual slow rhythmic waves. *E. S. Fountain*

335. **Digestive and Biliary Manifestations of Myopathies.** (Les manifestations digestives et biliaires des myopathies)
É. Fassio. *Presse Médicale* [*Pr. méd.*] **59**, 191–193, Feb. 14, 1951. 33 refs.

The author asserts that the myopathies are accompanied by cardiac and other visceral disturbances. This paper deals with the biliary and digestive disturbances in 8 patients, 3 of whom had myopathy of the Leyden-Moebius type and one each of whom suffered from conditions described as: the Landouzy–Déjérines and Erb syndromes, myopathy with Cushing's syndrome, myopathy with Bickel's hypopituitarism, and "myopathy with bilateral coxo-femoral syndrome and terminal azotemic psychogenic encephalitis" [!]. The observation and investigation of these cases included radiology of the gastro-intestinal tract and of the gall-bladder, with studies of hepatic and endocrine function.

These observations revealed that there is a phenomenon of digestive and biliary atonia. This may manifest itself either as an acute abdominal syndrome with epigastric right hypochondrial, or iliac pain or, more commonly, as one of a number of sub-acute or chronic abdominal conditions. The clinical accounts are rather brief and in telegraphic language, but it appears that in addition to the pains mentioned the patients may also suffer from aerophagy and meteorism, or alternatively constipation and diarrhoea and other vague abdominal discomfort. In one case atonia of the gall-bladder was demonstrated radiologically.

No pathological material being available, the way is left open for a lengthy discussion of the pathological physiology. The smooth-muscle tissue and the neuromuscular junctions are primarily at fault, but the guilty triad is completed by dysfunction of neuro-endocrine origin. These pathogenic deductions depend for their confirmation, to a large extent, on the claimed therapeutic success of a series of drugs classified as muscular, nervous, and hormono-vitaminic in effect. The author prescribes 5 ml. of 5% glycine intramuscularly every other day, acetyl β-methylcholine bromide 50 mg. twice daily, and neostigmine 4 tablets daily for periods of 10 days at a time; the length of the intervals between these courses is not indicated. These drugs are designed to overcome the disturbance of smooth-muscle function and of the neuromuscular junctions. The neuroendocrine disturbances are treated variously with thyroid, pituitary, and ovarian hormones in unstated dosage. In addition to this hormonal support, vitamin aid is secured with 25 mg. of aneurin every other day and 50 mg. of α-tocopherol six times daily. *L. A. Liversedge*

336. **The Incidence and Heredity of Muscular Dystrophy. A Study of Seventy-one Patients Admitted to the Massachusetts General Hospital**
M. R. BROWN. *New England Journal of Medicine* [*New Engl. J. Med.*] **244**, 88–90, Jan. 18, 1951. 1 fig., 4 refs.

At the Massachusetts General Hospital between 1870 and 1947 a diagnosis of progressive muscular atrophy was made in 71 instances. The series consisted of 47 males and 24 females. Only 6 cases were diagnosed during the period 1870 to 1916. In contrast, 35 cases were investigated between 1937 and 1947. Although the increase in the incidence of the disease is attributed to the increase in the foreign-born population, there is no evidence that the disease is peculiar to any particular race. Progressive muscular atrophy was found in the siblings of 14 patients, but no patient had either a parent or a child with the disability. Some patients had pseudohypertrophic muscles; others suffered from generalized muscular atrophy, with the initial lesion in the thighs. In a third type of case the generalized atrophy was first detected in the scapulo-humeral musculature. Among the patients with facio-scapulo-humeral dystrophy there appeared to be no evidence of dominant descent from parent to child. The inheritance was recessive in all types of dystrophy. Thirteen patients had other hereditary defects, including pes cavus, feeblemindedness, and progressive nerve deafness.

Early onset of dystrophy seemed to herald the advent of severe disablement. This phenomenon was more often observed in males than in females. Hormone therapy was found to be ineffective. In one case the administration of adrenocorticotrophin (ACTH) resulted in a transient increase in muscle weakness. Attention is drawn to the case of a male, aged 24 years, who had suffered from the disease since the age of 8 years. Necropsy revealed the presence of cardiac enlargement, mural thrombi in the left ventricle, and infarcts of the kidneys and spleen. Microscopical examination demonstrated that both the myocardium and the dystrophic skeletal muscles were affected by fibrosis and fatty infiltration. *A. Garland*

CENTRAL NERVOUS SYSTEM

337. **Subdural Effusions Complicating Bacterial Meningitis**
M. H. D. SMITH, R. E. DORMONT, and G. W. PRATHER. *Pediatrics* [*Pediatrics*] **7**, 34–43, Jan., 1951. 2 figs., 22 refs.

The successful treatment of bacterial meningitis has provided opportunities for observing certain sequelae of such affections. This article records the discovery of 20 cases of subdural effusion in 43 patients under 2 years of age suffering from bacterial meningitis, caused by *Haemophilus influenzae* in 17, by *Streptococcus pneumoniae* in 16, and by *Neisseria meningitidis* in 7. The effusions were discovered usually during the second week, and in 15 of the 20 at the first subdural "tap". Subdural taps were carried out at the two lateral angles of the anterior fontanelle. The fluid obtained varied in appearance from xanthochromic to blood-stained or purulent, and in quantity from 2 to 75 ml. In 3 cases bacterial culture of the fluid obtained was positive. Once discovered, the subdural fluid was drained by repeated puncture until little or no further fluid was obtainable and the patients seemed clinically improved. The authors advise routine tap once or twice in all children recovering from meningitis, since 9 of these effusions were discovered unexpectedly, although in the other 11 cases convulsions, focal signs, fever, chronic meningitis, bulging fontanelle, or other signs of increased pressure were also present. They feel sure that the fluid is not the result of the tap itself since in most cases fluid was present on the first tap, while less than 1 ml. of clear fluid is present in the normal subdural space. The aetiology of subdural effusions in general is considered and an analogy is made between subdural and pleural effusions. *Fergus R. Ferguson*

338. **Prolonged Abnormality of Cerebrospinal Fluid after Cisternal Streptomycin**
D. BEYNON. *Lancet* [*Lancet*] **1**, 322–324, Feb. 10, 1951. 1 fig., 7 refs.

A case is described of severe acute meningitis due to *Bacterium faecalis-alkaligenes*, a very rare and fatal infection, in a baby aged 6 weeks. Treatment was with streptomycin, cisternal as well as intramuscular, because of spinal block. Recovery was rapid, but a mild abnormality of the cerebrospinal fluid, in the form of raised protein level, persisted for over 23 weeks. This is considered to be a direct toxic effect of streptomycin, but has been without any ill effects on the patients, as judged by clinical examination after an interval of nearly 2½ years. A possible effect of streptomycin in producing raised intracranial pressure is also discussed.—[Author's summary.]

339. **Seizure Patterns in Psychomotor Epilepsy**
L. M. GOLUB, H. V. GUHLEMAN, and J. K. MERLIS. *Diseases of the Nervous System* [*Dis. nerv. Syst.*] **12**, 73–76, March, 1951. 3 refs.

A study is described of seizure patterns in psychomotor epilepsy. Although a focus of spike seizure activity in the anterior portion of the temporal lobe is found in the electroencephalogram of patients with seizures classified as psychomotor epilepsy, it is often difficult to decide on clinical grounds to what a given example of bizarre behaviour should be attributed. It was thought that a study of a group of patients manifesting paroxysmal episodes of non-convulsive behaviour disturbance with complete or partial amnesia, and showing anterior temporal spikes or sharp wave activity in the inter-seizure electroencephalogram, might give valuable information. A group of 21 patients having psychomotor attacks, either alone or combined with grand mal or focal motor seizures, was studied: 4 patients showed evidence of structural brain pathology, 3 others had psychotic manifestations, 6 had definite personality disorders, 1 had a history of sleep paralysis, and 1 a congenital reading disability. It was found that three phases of activity occurred in the attacks: (1) a

suspension of activity, as seen in petit mal; (2) repetitive, stereotyped activity, such as lip smacking, licking or rubbing, picking at clothing, or erratic, repetitive movements of arms or legs; (3) complex, semi-purposeful, and variable behaviour involving interplay with environment, gradually merging into normal behaviour. As the manifestations of the third stage may be post-ictal in nature, it is suggested that psychomotor seizures should not be defined in terms of these. *Myra Mackenzie*

340. **Unusual Aurae in Two Cases of Epilepsy in Childhood**
B. D. WYKE. *British Medical Journal* [*Brit. med. J.*] **1**, 272–275, Feb. 10, 1951. 3 figs., 18 refs.

The author describes 2 cases of epilepsy in which there were unusual aurae. In the case of a girl aged 6 the unusual " aura " was profuse salivation followed by unexpected vomiting; this was succeeded in turn by loss of consciousness, twitching of the whole body, tongue biting, and occasionally incontinence. These attacks occurred about 6 times each year. In the second case, in a boy of 11, the seizures all occurred in the night or early morning and were preceded by a visual aura in which he saw " hundreds of objects ranged behind one another ". These objects consisted of some article of furniture at which he was gazing at the time the fit began, and each object seemed bigger than the one in front. The aura was not experienced in the absence of illumination and the object had to be seen for the phenomenon to occur. The seizures were characterized by smacking of the lips and turning of the head and eyes to the right. It is suggested that both these cases raise the possibility of temporal-lobe affection; focal electroencephalographic changes were absent.

[Two points seem worthy of comment: vomiting is not, strictly speaking, an " aura ", which is essentially a subjective phenomenon; although reference is made to the aura of the second patient as " organized visual hallucinations ", this is not really the case since some real visual stimulus was required to produce this illusion of " hundreds of objects ".] *L. A. Liversedge*

341. **Basilar Impression of the Skull**
J. E. A. O'CONNELL and J. W. A. TURNER. *Brain* [*Brain*] 73, 405–426, 1950. 22 figs., 36 refs.

Basilar impression of the skull is the term used to describe an invagination of the upper cervical spine into the posterior fossa. The term " platybasia " is sometimes used, but this is inexact. The authors review the historical aspect briefly and proceed to record 5 cases; the age of onset varied from birth to 40 years; symptoms began insidiously, in 2 cases being precipitated by injury, and were slowly progressive. There are four main types of neurological picture, and in the majority of cases combinations of these types occur: (1) hydrocephalus and raised intracranial pressure; (2) bilateral cerebellar disturbance; (3) interference with the function of the lower cranial nerves; and (4) spinal-cord compression at the level of the foramen magnum. Of the major presenting symptoms, cervical pain is important. On examination, the most characteristic abnormality is shortness of the neck, with the external occipital protuberance approaching the vertebra prominens. Cranial nerve palsy is common, and in 4 of the authors' cases cerebellar disturbance occurred.

Treatment was by means of what is essentially a suboccipital craniotomy with removal of the arch of the atlas and a wide opening of the dura. Good results followed, particularly in the more recent of their cases, and the authors feel that surgery can do much for these cases and urge earlier diagnosis and treatment.

Aetiologically the cases fall into two groups, the secondary ones, where the condition is consequent on a softening of the base of the skull allowing the weight of the head to cause the skull to sink downwards, and the others, classed as primary, where there is no bony disease and the condition is regarded as a congenital developmental abnormality. These cases may be associated with other skeletal deformities, such as Klippel–Feil deformity or spinal bifida. *N. S. Alcock*

342. **The Syndrome of Lamellar Cerebellar Degeneration associated with Retinitis Pigmentosa, Heterotopias, and Mental Deficiency, with Report of a Case**
P. B. HAGEN, K. B. NOAD, and O. LATHAM. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 217–223, Feb. 10, 1950. 13 figs., 28 refs.

The main interest of this case lies in the question whether the lesions found were the result of a degenerative process or whether this process was superimposed on a developmental anomaly. The patient was a man who died at the age of 73 years after having had difficulty in walking and a speech disorder from the age of 8 years. He had always been of subnormal mentality and could neither read nor write. When first observed, at the age of 69, his speech was suggestive of a cerebellar lesion, his gait was ataxic, and irregular movements were seen in the arms. An intention tremor was also present. The deep reflexes were recorded as " exaggerated ", but no note was made of any other abnormality of the legs. The cerebrospinal fluid was normal. On examination 2 years later bilateral immature cataracts were found which obscured the fundi. Bilateral abducens paralysis was present. On this occasion the knee and ankle jerks were recorded as brisk and equal and the plantar responses as flexor. The patient died 2 years afterwards of generalized peritonitis following rupture of the appendix.

At necropsy the cerebellum was very small, weighing only 46·5 g. as compared with an average normal of 156 g. No abnormality was noticed macroscopically in the cerebral hemispheres. Histologically, sections of the retina revealed severe degeneration with some pigmentation, the degeneration being most severe in the middle zone. In the cerebral cortex many degenerate nerve cells were found in the second and third layers, accompanied by marked gliosis. Argentophile plaques were found in every area examined, though these were not as numerous as in Alzheimer's disease. In the medulla the inferior olivary nuclei had suffered severe atrophy, only a few scattered nuclei remaining. The cerebellar lesions consisted of almost complete demyelination of

the foliae, thinning of the granular and molecular layers with glial replacement, and almost complete absence of the Purkinje cells. Not one normal Purkinje cell was to be seen; those present were devoid of processes. There was great proliferation of the Bergmann glial cells which, with their tangled strands of processes, produced a " bush-like " appearance. The granular layer had been replaced by glial cells and in the midst of these were large numbers of Golgi Type-2 nerve cells. Numbers of similar cells were seen in the molecular layer. Although the abnormally small cerebellum found at necropsy, together with the history of ataxia from an early age, suggests a developmental anomaly, the fact that remains of Purkinje cells were found, that the dentate nuclei and cerebellar peduncles were well preserved, and that the degenerative condition of retinitis pigmentosa was associated with the disease process leads the authors to postulate the existence of a degenerative process superimposed on a developmental background. *Ruby O. Stern*

343. **The Clinical Picture of So-called Idiopathic Bilateral Athetosis, with Description of a Case.** (Das klinische Bild der sogenannten idiopathischen bilateralen Athetose. Ein kasuistischer Beitrag)
W. KOSENOW. *Zeitschrift für Kinderheilkunde* [*Z. Kinderheilk.*] **69**, 285–304, 1951. 5 figs., 44 refs.

Idiopathic bilateral athetosis is comparatively rare and very little has been published on the pure form of this disorder. The author describes in detail the case of a 6½-year-old boy, stressing the typical clinical signs which differentiate this encephalopathy from those associated with extrapyramidal symptoms. The patient had severe jaundice at the age of one month and whooping-cough complicated by pneumonia at 5 months, but without indication of encephalitis. Physical development was extremely slow, and at the age of 3 years he was unable to sit, stand, or speak. At that time he developed weakness of the right leg and hypersensitivity of the right foot; these were transitory, although marked shortening of the right leg resulted, and were believed to be due to a slight attack of poliomyelitis. Although his mental development was normal, he made little progress in the following years in walking and speech, and gradually developed strange and uncoordinated movements. When admitted to hospital at 6½ years his general condition was satisfactory, but bizarre involuntary movements were observed, involving the neck, face, arms, and legs. He was able to sit, but could stand only by holding the bed rail. He needed assistance when walking. When asked to carry out a definite action, such as pressing a bell button, the movements increased enormously in extent, his right arm approached the bell button with uncontrolled movements, bent at right angles at elbow and wrist, and he was unable to press the button with his index finger, but had to resort to the use of all his fingers, which were fixed in a spastic position. Speech was greatly impeded, only the words " yes " and " no " being clearly enunciated, and again when trying to speak his whole body seemed to participate. This also occurred when he tried to eat without assistance; when fed, however, he was able to masticate and swallow almost normally. When at rest no abnormal condition was noticeable but at the slightest provocation the bizarre movements occurred again. Intelligence tests showed normal mental development, and there were no significant abnormal findings in the central nervous system. The air encephalogram, however, showed asymmetry and slight enlargement of the frontal part of the lateral ventricles. The electroencephalogram was not quite normal, α-waves not being obtainable from the occipital regions and the rapid frequencies predominating.

The author discusses the differential diagnosis and pathogenesis of idiopathic athetosis, and concludes that although it is believed to be an exclusively extrapyramidal disease, it should still be considered to fall in the category of infantile encephalomyelitis. *E. S. Fountain*

344. **Lysivane and Artane in the Treatment of Parkinsonism**
O. GARAI. *Lancet* [*Lancet*] **1**, 429–432, Feb. 24, 1951. 6 refs.

This is a report of the use of " lysivane ", or ethopropazine, (a synthetic drug allied to promethazine and diethazine) and " artane " (benzhexol, a synthetic piperidyl compound) in the treatment of Parkinsonism. A total of 70 patients were studied; 51 received artane, 43 lysivane, and 24 both compounds. The trial has lasted a year, but because of the steady influx of new cases not all have been observed for this period. Assessment was purely on clinical grounds: more than half the cases were post-encephalitic, the rest being idiopathic except for 2 arteriosclerotics. There was no great difference between results in each group.

With lysivane, of the 43 patients, 3 were greatly, 16 moderately, and 12 slightly improved; in 9 there was no change; and 3 were worse. Toxic symptoms were noted in 24 patients, in 9 of whom the drug had to be discontinued. Of the toxic symptoms the most prominent were drowsiness, ataxia, confusion, blurred vision, giddiness, and depersonalization. Full details of dosage are not given, but in 3 typical cases it was 50 mg. 3-hourly, 1,500 mg. a day, and 500 mg. a day respectively.

With artane, of 51 patients, 8 were greatly, 20 moderately, and 10 slightly improved; in 11 there was no change; and 2 were worse. In 19 there were toxic symptoms and in 3 the drug had to be discontinued, but the toxic effects were much less troublesome than with lysivane. Chief toxic complaints were giddiness, dry mouth, depersonalization, nausea, and blurred vision. The dosage was 60 to 100 mg. daily, though the average was about 50 mg. daily. In most cases it was found necessary to exceed 50 mg. before full benefit was obtained. In many post-encephalitic cases amphetamine had a potentiating effect on artane. Both drugs controlled the rigidity better than the tremor, and both helped in oculogyric crises.

[Every new treatment for Parkinsonism has been introduced with figures of improvement, as here also, in the region of 70%. None has so far stood the test of time.] *N. S. Alcock*

Psychiatry

345. Intravenous Pervitin and the Psychopathology of Schizophrenia

J. M. HOPE, E. CALLAWAY, and S. L. SANDS. *Diseases of the Nervous System* [*Dis. nerv. Syst.*] **12**, 67–72, March, 1951. 3 figs., 11 refs.

The effects are described of intravenous " pervitin ", the D-isomer of desoxyephedrine (known also as " DOE ", " desoxyn ", and " methedrine "), on 30 selected hospital patients with schizophrenia, aged 18 to 54 years (mean age 33), in Worcester, Massachusetts. The time between admission to hospital and study varied from 1 month to 33 years (mean 2 years). The group was divided into 3 sub-groups, 5 males and 5 females in each, one sub-group being predominantly catatonic, another overtly paranoid, and the third chosen without regard for special symptoms. Though the psychiatric rating scale used, that of Malamund and Sands, includes 22 functions, only 16 were considered necessary for the present study as the effects of pervitin were immediate and lasted for only 30 to 45 minutes in some cases. The mental status of each patient was first evaluated, then 20 mg. of pervitin in 1 ml. of an aqueous isotonic solution was rapidly injected intravenously. All but 2 patients showed marked change of some kind after the injection. In general the patient became more communicative and showed a reaching out for contact with the examiner; in some cases strong emotion was shown or delusional material and pathological thought processes were more accentuated or more accessible. None of these changes lasted after the effect of pervitin had worn off, and no clinical improvement occurred. But as the schizophrenic " process " had been influenced by a chemical agent it was considered that further study on these lines might shed light on the nature of psychiatric disease processes in general.

Myra Mackenzie

346. Value of Convulsive Therapy in Juvenile Schizophrenia

S. LEVY and R. H. SOUTHCOMBE. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **65**, 54–59, Jan., 1951. 11 refs.

The value of convulsive therapy in juvenile schizophrenia is discussed. The cases of all patients under 18 years with a diagnosis of schizophrenia admitted for the first time to Eastern State Hospital, Medical Lake, Wash., since 1891 are reviewed. Of 14,858 patients admitted since that time, 291 were under 18 years old. Hospital and follow-up records of this group were carefully checked, as also were the diagnosis, treatment, adjustment during hospital stay, and adjustment to society after release. Special attention was paid to the treatment given to juvenile patients. In Eastern State Hospital there were no special facilities for treatment of this group, which was mixed up with patients of all ages and shared the same routine. Of the 291 juveniles (187 males and 104 females), 103 were schizophrenics, an incidence of 36% among all juvenile patients. The incidence of schizophrenia among all admissions to the hospital was approximately 28%. Of the 103 juveniles with schizophrenia, 4 were between 10 and 12, 14 between 12 and 15, and 85 between 15 and 18 years of age. In 1936 new methods of treatment were started at Eastern State Hospital, and all the 47 patients with juvenile schizophrenia admitted since then have received such special treatments as prolonged narcosis, convulsive shock with picrotoxin, leptazol, and the electric current, insulin shock, and narcosynthesis. Insulin shock was given in 41 of the 47 cases, either alone or as well as leptazol shock or electric shock. Eleven patients had at least one course of electric convulsion therapy consisting of 15 to 20 treatments, and all but one of the group received a full course of insulin shock as well. Insulin shock was given 5 times a week for approximately 13 weeks, the patient being left in full coma for one hour. All patients also received psychotherapy and occupational and recreational therapy.

Results of treatment were classified as good (ability to leave hospital and to live permanently an ordinary social life), fair (recovery from acute psychosis and ability to leave hospital on parole, but with liability to relapse), or poor (perhaps some slight improvement, but little real change in the psychotic condition). Of the 47 patients, 6 (13%) were able to leave hospital and live an ordinary life; in 10 cases results were fair or poor, and 31 received no benefit at all from the treatment. This compares unfavourably with the 31% recovery rate among adult patients receiving convulsion therapy. The recovery rate among the 56 juvenile schizophrenics untreated except by institutional care and occupational therapy was 16%.

It was concluded, in accordance with the findings of other investigators, that schizophrenia occurring before the age of 18 appears to be potentially chronic, tends to run a malignant course, and is not benefited by any of the convulsion therapies. *Myra Mackenzie*

347. A Central Homeostatic Mechanism in Schizophrenia

D. HILL, P. STJ. LOE, J. THEOBALD, and M. WADDELL. *Journal of Mental Science* [*J. ment. Sci.*] **97**, 111–131, Jan., 1951. 12 figs., 11 refs.

At the Maudsley Hospital the authors examined 17 normal subjects, aged 20 to 41 years, and 40 schizophrenics, 8 of whom underwent 108 experiments. The examination consisted of investigation of the blood sugar level during the 30 minutes after the intravenous injection, in the fasting state, of 0·5 unit of insulin per lb. (1·1 unit per kg.), with electroencephalographic, electrocardiographic, and palmar galvanic skin resistance

records. The controls showed 4 types of blood sugar response, and an inverse relationship between the heart rate and skin resistance was usually found. The changes found in 12 of 14 controls were a slowing of the alpha (occipital, 8 to 13 c.p.s.) activity followed by the appearance of a new rhythm at 5 to 6 c.p.s. in the frontal or central areas within ¼ to 3 minutes, a rapid fall in skin resistance and rise in heart rate, and a rise in blood sugar level 1 to 8 minutes later. The points in which patients differed from controls were: (1) blood sugar level at which 3 to 6 c.p.s. activity appeared was lower; (2) time at which this occurred was later; (3) the order of events was not constant (in 29 of 79 experiments the rise in blood sugar occurred before the changes in the electroencephalogram (EEG) or galvanic skin resistance (G.S.R.); (4) relationship between rise in blood sugar level, appearance of theta rhythm, and time of fall of G.S.R. was variable; and (5) correlation between absence of response in EEG, G.S.R., and heart rate to falling blood sugar level and catatonic stupor. The conclusions are that the theta rhythm is delayed; the excitability of the central sympathetic–adrenaline system is reduced; the process of depression of cortical function followed by discharge of the sympathetic system is defective; and the variations are related to the clinical state and are most apparent in catatonic stupor.

G. de M. Rudolf

348. **Aetiology of Gilles de la Tourette's Disease and the Problem of Regression.** (Beiträge zur Ätiologie der "Maladie Gilles de la Tourette" und zum Regressions-Problem)

J. HEUSCHER. *Schweizer Archiv für Neurologie und Psychiatrie* [*Schweiz. Arch. Neurol. Psychiat.*] **66**, 123–158, 1950. Bibliography.

The author makes an extensive survey of the aetiological, psychopathological, and clinical aspects of the syndrome described in 1885 by Gilles de la Tourette under the name of convulsive tic. The association of generalized tics with obsessive-compulsive behaviour, involuntary screaming, and echolalia and coprolalia is discussed and regarded as evidence of regression to a more primitive stage of mental development. The whole problem of regression is discussed at length and the author attributes to regression a biological meaning much wider than that of the psycho-analysts. Three cases are described in detail to illustrate the gradual transition which may occur between convulsive tics, obsessions, and schizophrenic states.

[This interesting paper deserves to be studied in its original form by anyone who wishes to take up the fascinating subject of convulsive tics; the paper also contains a valuable list of references.]

J. T. Leyberg

349. **Pneumoencephalographic Changes following Prefrontal Leukotomy (Freeman–Watts Technic)**

I. MESCHAN and J. B. SCRUGGS. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **65**, 60–71, Jan., 1951. 4 figs., 5 refs.

The pneumoencephalographic findings are described in 19 unselected cases before and after prefrontal leucotomy at the U.S. Veterans Administration Hospital, North Little Rock, Arkansas. These findings are correlated with observations at a few necropsies performed in this hospital and others.

Between May 21, 1947, and July 15, 1948, 19 patients (one a negro) underwent pneumoencephalography before prefrontal leucotomy, at an interval varying from several days to (in one case) 9 months. Post-operative studies on 19 men took place at any time between 4 and 20 months after the operation. The patients were aged 24 to 66 years, 7 being over 38 years. Except for one who had had a manic-depressive psychosis (manic type) for 22 years, all the patients were suffering from dementia praecox. The psychosis in all the 19 patients had lasted for more than 3 years, except for one who had been ill for only 9 months; 11 had had some form of shock therapy, without benefit, before the pneumoencephalographic study.

The pre-operative findings in 9 cases were normal or at the upper limit of normal. In 5 cases the ventricular system was normal, but there was an increase in the air (diffuse in 2 cases, localized in the frontal regions in 3) in the subarachnoid space surrounding the brain, accentuating the sulcal markings. In the remaining 5 cases the following abnormalities appeared: slight diffuse dilatation of the entire ventricular system and increased air around the cerebral cortex (1 case); well marked dilatation of the entire ventricular system only (1 case); slight lateral dilatation of the left ventricle, with increased sulcal markings on the left cerebral cortex (2 cases); questionable slight dilatation of the anterior horns of lateral ventricles only (1 case). Significantly, the sulcal markings were in no case obliterated, nor was the subarachnoid space surrounding the brain seen to be obliterated, but significant post-operative pneumoencephalographic changes were to be found in all the cases.

The post-operative findings were: progressive dilatation of all the ventricles, most pronounced in the anterior portions of the lateral ventricles; progressive apparent obliteration of the subarachnoid space surrounding the cerebral cortex (the commonest finding); development of porencephalic cysts in 5 (possibly 6) cases, in only one of which was the pre-operative pneumoencephalogram completely normal. Four other definite cysts developed in cases in which the ventricles were found dilated pre-operatively, hence the anterior horn of the lateral ventricle was probably penetrated at operation.

None of the patients in this series died: 7 patients out of the total of 85 undergoing prefrontal leucotomy in this hospital died, and necropsy was performed in 6 cases; a summary of the relevant pathological changes found in 5 of the cases is given. These included cystic necrosis of the frontal lobes; atrophy and gliosis throughout the brain; meningeal thickening, scarring, and haemorrhages; generalized enlargement of the ventricles, most obvious in the frontal horns; and cystic degeneration of the thalamus and basal ganglia, particularly in the nucleus medialis dorsalis of the thalamus.

As porencephalic cysts occurred more frequently in cases in which dilatation of the anterior horns of the lateral ventricles was present pre-operatively, the authors

consider that this is due probably to more ready penetration of the anterior horns by the leucotome. They suggest that pre-operative pneumoencephalography should be carried out in all cases of prefrontal leucotomy; should dilatation of the anterior horns be found, the surgical technique must be modified accordingly.

Myra Mackenzie

350. **Immediate Effects of Shock Therapies, Epinephrine and ACTH on Blood Glutathione Level of Psychotic Patients**

D. H. HENNEMAN and M. D. ALTSCHULE. *Journal of Applied Physiology* [*J. appl. Physiol.*] **3**, 411–416, Jan. 1951. 1 fig., 10 refs.

The concentration of reduced glutathione in the erythrocytes was determined in psychotic and severely neurotic patients before and after electric convulsion therapy, ambulatory insulin therapy, or the injection intramuscularly of 0·1 ml. of adrenaline per kg. body weight or of 25 mg. of adrenocorticotrophin (ACTH). The blood glutathione level was increased by 20 to 150% in 20 patients 2 to 4 hours after electric shock treatment. A similar rise of 16 to 54% occurred after adrenaline injections in 15 patients. A smaller and less consistent increase was found after ambulatory insulin treatment and ACTH injections. *F. K. Taylor*

351. **Permanency of Glutamic Acid Treatment**

F. T. ZIMMERMAN and B. B. BURGEMEISTER. *Archives of Neurology and Psychiatry* [*Arch. Neurol. Psychiat., Chicago*] **65**, 291–298, March, 1951. 18 refs.

[This paper is of interest, but must be read in its entirety for the reader to be able to judge its value and the value of this treatment.] *G. de M. Rudolf*

352. **Eosinophile Levels in Hospitalized Psychotics during Combined Testosterone–Oestrogen Therapy**

R. R. SACKLER, M. D. SACKLER, A. M. SACKLER, D. GREENBERG, J. H. W. VAN OPHUIJSEN, and CO TUI. *Proceedings of the Society for Experimental Biology and Medicine* [*Proc. Soc. exp. Biol., N.Y.*] **76**, 226–228, Feb., 1951. 2 figs., 13 refs.

353. **Loss of Written Language due to Dissolution of the Phonetic Structure of the Word in Brain Abscess**

R. KLEIN. *Journal of Mental Science* [*J. ment. Sci.*] **97**, 328–339, April, 1951. 22 refs.

354. **Visual Hallucination of the Self**

J. LHERMITTE. *British Medical Journal* [*Brit. med. J.*] **1**, 431–434, March 3, 1951.

The author suggests that it is now possible to carry out deep research on the phenomenon of autoscopy, the vision of one's double, the visual hallucination of the self. The vision appears with suddenness, while the person is wide awake, or more often when lost in thought or drowsy. Sleepiness seems specially favourable; the state of authentic dream is exceptional. The dreamer's image comes with a deep feeling of sadness or with deadly anxiety. Usually it is very clear, but not vivid in colour. The image retreats when approached or fades away after performing movements similar to those of the original. The hallucinatory image may appear very thin and of a jelly-like or glass-like substance, or opaque. Those experiencing the hallucination are not always immediately convinced of its reality, but finally it becomes compelling. One characteristic peculiar to autoscopy is noted: the subject knows that in the image there is part of himself, which thinks and feels like himself. Anxiety is often important as a source of the phenomenon. There are cases of prolonged duration and of frequent repetition of the bodily image. The "double" is well known as a theme in literature; the author lists several writers in whose works it is to be found, and discusses the connexion between literary genius and abnormality. The autoscopic vision of the double occurs in many diseases of the central nervous system—epilepsy, general paralysis, encephalitis, encephalosis of schizophrenia, focal lesions of the brain, and post-traumatic disorders.

Only from a study of the work of Head and Schilder is it possible to begin to understand the phenomena. Head and Holmes demonstrated the contribution of the postural attitudes to the knowledge of the position of our limbs. Investigations relating to body image indicate that at the boundary of our consciousness is the notion of our physical personality. If this can disappear or be distorted through the various diseases of the nervous system, it can also release itself partly from its natural frame to become an hallucination.

[No bibliography is given, but the author makes reference in the text to the work and cases of many others.]

John C. Kenna

355. **The Outcome of Mental Breakdown in Old Age**

F. POST. *British Medical Journal* [*Brit. med. J.*] **1**, 436–440, March 3, 1951. 1 fig., 11 refs.

An analysis was made of the records of all patients over 60 admitted to a mental observation unit in South London from February to May, 1946. Of 454 persons admitted, 105 men and 121 women were over 60, but 12 patients with primarily physical disease were excluded from the study. The remainder (214) were divided into two broad diagnostic categories: 26 men and 30 women were suffering from essentially "functional" (schizophrenic or affective) psychosis, while 69 males and 89 females exhibited organic mental symptoms.

A table shows the numbers of each category dying under hospital care; discharged; and remaining in hospital. The follow-up over 3½ years revealed striking differences in discharge and death rates of the two groups. Only a small proportion of old people suffering from mental breakdown occupy hospital beds for prolonged periods, those remaining after a year being about one-quarter. The results of a follow-up from records are given and a comparison is made with the findings of Clow (*N.Y. St. J. Med.*, 1948, **48**, 2357) and of Camargo and Preston (*Amer. J. Psychiat.*, 1945, **102**, 168). A table of age distribution and mortality is given.

To assess the importance of social factors in causation and outcome of mental breakdown in this group, 190

patients with no previous psychiatric breakdown were reviewed. A table shows the type of illness, marital status, and degree of social integration of these 190; the results are compared with those of Rowntree (*Old People*, London, 1947).

Although only 3% of the elderly population is estimated to live in institutions and homes for the aged, 17·4% of these patients had passed through public assistance institutions. This point is discussed. Persons admitted from institutions or from a lonely existence are older as a group than patients who had remained socially integrated.

The author concludes that the degree of social integration appears to have little influence on the outcome of mental breakdown. *John C. Kenna*

356. **Blood-groups of Mental Defectives and their Maternal Parents**
A. M. PANTIN. *Nature* [*Nature, Lond.*] **167**, 76, Jan. 13, 1951. 8 refs.

A random sample of 370 mental defectives in East Anglia was studied: of these, 252 were considered to be "undifferentiated" in that no obvious cause for the deficiency was found. The blood groups of these 252 and their mothers were determined using anti-A, B, C, D, E, and c sera. Of the total, 44·8% were group O, 46·4% group A, 6·0% group B, and 2·5% group AB. This confirms Race's findings of a slight excess of group A over group O in East Anglia. In 55 cases mother and child were ABO-incompatible: 191 children were D-positive and 61 dd. This is considered to be a statistically significant high figure for dd: 195 mothers were D-positive and 57 dd. In only 24 cases was the child D-positive and the mother dd. These figures do not suggest that ABO or rhesus incompatibility between mother and child is a significant cause of mental deficiency.
G. Jacob

357. **Psychic Complications of Influenza.** (Sulle complicazioni psichiche della influenza)
L. BIASCI. *Rivista Sperimentale di Freniatria* [*Riv. sper. Freniat.*] **74**, 573–588, Dec. 31, 1950. 19 refs.

Psychotic manifestations were studied in 6 cases of influenza admitted to the Clinic for Nervous and Mental Diseases of the University of Pisa during the influenza epidemic of 1948–9. In all 6 patients the onset of the psychosis occurred during the period of convalescence. There was one case each of confusional psychosis with depressive features (which recovered after 8 sessions of electric convulsive therapy (E.C.T.)), depression (treated with sedatives), acute hallucinatory delirium (also treated with sedatives), schizophrenia (which received 8 bouts of E.C.T. and 30 insulin comas with little benefit), exhaustion psychosis (which recovered after 8 bouts of E.C.T.), and dissociative syndrome (treated with 28 insulin comas). The course of the illness, except in the case of schizophrenia, was generally short (about one month). All patients were discharged recovered, barring the one suffering from schizophrenia, whose condition has become progressively worse. Five out of the 6 patients were women between the ages of 30 and 40 years. The author found evidence of heredity of mental disorder in only one of his cases (the father of the patient suffering from an acute hallucinatory delirium had committed suicide, and a brother had attempted suicide). The patient manifesting a confusional state with depressive features had had an attack of mental disorder of an unknown nature some 4 years previously.

The author concludes that influenza may give rise to various clinical forms of mental disorder, and takes the view, shared by other workers, that the mental changes are produced by the neurotropic action of the influenza virus on the cerebral nerve cells. *P. Cassar*

358. **The Psychopathology of Ovulation and Menstruation.** (Die Psychopathologie der Ovulation und Menstruation)
A. HUTTER. *Schweizer Archiv für Neurologie und Psychiatrie* [*Schweiz. Arch. Neurol. Psychiat.*] **66**, 159–172, 1950. 2 figs., 4 refs.

The relation between ovulation, menstruation, and affective disorders is generally recognized, but insufficient attention has been paid to the association of menstrual changes with the outbreak and the course of other psychoses. The author describes a case of schizophrenia in which acute paranoid and catatonic disorders were always precipitated and aggravated by menses. The psychopathology of this group of psychoses, which the author calls "menstrual psychoses", is discussed.
J. T. Leyberg

359. **Mental Disorder and Other Psychiatric Problems in Pellagra.** (La psychose pellagreuse et les problèmes psychiatriques)
B. LLOPIS. *Schweizer Archiv für Neurologie und Psychiatrie* [*Schweiz. Arch. Neurol. Psychiat.*] **66**, 172–192, 1950. 29 refs.

In the author's extensive experience with pellagrins during the Spanish war, mental disorders were commonly encountered. They belong to the group of Bonhoeffer's "exogenous reactions". The clinical syndromes may vary considerably according to the severity of the avitaminosis. As a rule the psychosis passes through the following stages: a mild neurasthenia-like reaction, a more severe affective disorder (manic, depressive, or paranoid) followed by oneiriform clouding of consciousness, and finally profound dementia. These syndromes are non-specific and, despite their aetiology, indistinguishable from typical schizophrenia or other so-called "endogenous psychoses". These observations made on pellagrins serve the author with a starting point in discussing the relationship between endogenous and exogenous reactions. The part played by clouding of consciousness in the occurrence of hallucinations and other psychopathological manifestations is particularly stressed. An attempt is made to present most of the psychiatric symptoms on an organic basis and to associate them with selective disturbance of consciousness and impairment of such perceptive functions as keep the individual in close touch with reality. *J. T. Leyberg*

Infectious Diseases

360. **Personal Description of a Case of Weil's Disease.** (Spostrżezenia dokonane na sobie samym w przebiegu choroby Weila)
R. Orliñski. *Polski Tygodnik Lekarski* [*Polsk. Tyg. lek.*] **5**, 1281–1286, Sept. 4, 1950. 15 refs.

[The symptoms and course of the case of Weil's disease described should be specially interesting as they were recorded by the patient, a medical man.]

The course was severe, all the symptoms of an infectious disease being present; these included loss of hair, disturbance of vision because of haemorrhagic retinitis, bleeding, rapid loss of weight, and jaundice. The kidneys were not seriously affected. Repeated examinations of urine, as well as inoculation of guinea-pigs, failed to confirm the clinical diagnosis. The only positive serological reaction was obtained with the patient's serum taken a little more than one month after the onset of the disease. This sample of serum, taken on the 33rd day of disease, produced a positive reaction with a laboratory strain of *Leptospira icterohaemorrhagiae* in a dilution of 1 in 25,600 and with a strain of *L. canicola* in dilution of 1 in 3,200.

The author recommends treatment with penicillin in high doses. This treatment leads to a fall in the previously high temperature in 36 hours, and a rapid improvement in the symptoms. Penicillin, however, had no effect on the ocular disturbances or the intensity of jaundice. The infection was contracted from bathing in a lake, the symptoms appearing 10 days afterwards.

J. W. Czekalowski

361. **Q Fever in California. III. Aureomycin in the Therapy of Q Fever**
W. H. Clark, E. H. Lennette, and G. Meiklejohn. *Archives of Internal Medicine* [*Arch. intern. Med.*] **87**, 204–217, Feb., 1951. 5 figs., 7 refs.

Aureomycin was given to 43 patients with Q fever. The drug was given in a dose of 1 to 5 g. per day, by the oral route to 25, orally and parenterally to 17, and by the parenteral route only to 3 patients. The duration of fever from the commencement of therapy was chosen as the main criterion for evaluating the clinical response. The results with aureomycin were compared with those obtained in a separate series of 25 patients who received penicillin and who were similar in respect of age, sex, and duration of illness before treatment.

The median duration of fever in the aureomycin-treated series was 3 days, and in the penicillin-treated series 8 days. Fever persisted for periods ranging from 7 to 33 days from the initial dose of aureomycin in 13 cases, but in 9 of these subjective improvement occurred within 48 to 72 hours. The other 4 cases were not benefited in any way by treatment with aureomycin. More than half of the patients in the aureomycin-treated groups showed symptoms of drug toxicity in the form of gastro-intestinal upset. Penicillin appeared to have little or no effect on the course of the disease. In both groups there were several patients in whom a satisfactory response was considered to be coincidental with antibiotic therapy.

The diagnosis of Q fever was confirmed in all 60 patients by means of specific complement-fixation and agglutination tests, or by the occurrence of a rickettsiaemia. The presence of rickettsiae in the circulating blood was demonstrated by inoculating guinea-pigs with whole blood from the patient and testing for specific antibodies in the animals' serum. Rickettsiaemia was demonstrated in 5 patients while they were receiving treatment with aureomycin; blood samples from 2 patients were found to contain rickettsiae, although the aureomycin concentration in the serum was as high as 9·9 mg. per ml.

The authors conclude that there is a place for aureomycin in the treatment of Q fever, but they admit that the effect of the drug in many cases of the disease is slight or negligible.

G. B. Forbes

362. **Hydatid Disease (Echinococcosis) in Alaska and the Importance of Rodent Intermediate Hosts**
R. Rausch and E. L. Schiller. *Science* [*Science*] **113**, 57–58, Jan. 19, 1951. 1 fig., 4 refs.

363. **Hemoglobin Determination in Hookworm Disease Case-finding**
P. C. Beaver. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **31**, 90–97, Jan., 1951. 21 refs.

The control programme in Georgia for hookworm disease is based on the selection of anaemic school-children for stool investigation. The study reported is an attempt to establish the normal range of haemoglobin level in school-children and to determine the correlation, if any, between anaemia and infection. Haemoglobin estimations were carried out on 1,307 white children in a rural area in Georgia where hookworm infection is endemic, and on 1,174 urban children in an almost hookworm-free area. On the basis of the findings in the urban areas, in children of 6 to 10 years and in older children the borderline levels were found to be 10·0 g. and 11·0 g. per 100 ml. respectively, lower levels indicating frank anaemia. Of 40 anaemic patients only 3 were negative for hookworm, and of 74 borderline cases, 15 were negative. All children with egg counts above 20,000 eggs per ml. and half of those with counts between 5,000 and 20,000 were in the anaemic or borderline class, whereas only 13% of those with counts of less than 5,000 had low haemoglobin levels. Thus if hookworm disease case-finding is confined to anaemic persons, very heavily infected cases will be detected but a large number of more lightly infected cases will be missed.

J. L. Markson

364. **Tick Paralysis: Implicating *Amblyomma maculatum***
R. S. PAFFENBARGER. *New Orleans Medical and Surgical Journal* [*N. Orleans med. surg. J.*] **103**, 329–332, Feb., 1951. 9 refs.

Tick paralysis results from a tick bite—usually a tick of the *Dermacentor* variety. The clinical course is that of a rapid ascending paralysis, with cranial-nerve involvement in ascending order, and less frequent sensory changes. Death may result from respiratory failure, but recovery is usual if the tick is removed before bulbar symptoms appear. The absence of cerebrospinal-fluid changes differentiates the condition from poliomyelitis and infective polyneuritis. The nature of the toxic agent is unknown.

In the present paper two cases are described from widely separated areas in Louisiana, the tick in one case being identified as *Amblyomma maculatum*, which has not hitherto been associated with the condition. The writer emphasizes the importance of searching for ticks in cases of unexplained acute flaccid paralysis.

J. L. Markson

365. **Confusing Aspects of Infectious Mononucleosis**
D. A. GOLDTHWAIT and J. E. ELIOT. *American Journal of the Medical Sciences* [*Amer. J. med. Sci.*] **221**, 264–269, March, 1951. 1 fig., 35 refs.

During an investigation of possible haematological changes associated with exposure to cold, the finding of abnormal mononuclear cells in many of the blood films led to the discovery of a probable epidemic of infectious mononucleosis in 26 men sent to the Arctic. Only 5 men developed symptoms, of whom one had positive heterophile agglutinations together with liver damage and splenomegaly. The abnormal mononuclear cells were observed 30 to 131 days before the onset of symptoms. The significance of the absence of one or more of the three diagnostic criteria—reticulo-endothelial hyperplasia, abnormal mononuclear cells, and a positive heterophile agglutination—in symptomatic and asymptomatic cases is discussed. *I. Ansell*

VIRUS DISEASES

366. **Infection and Immunity in Smallpox**
A. W. DOWNIE. *Lancet* [*Lancet*] **1**, 419–422, Feb. 24, 1951. 2 figs., 19 refs.

In this University of London lecture new light is shed on the pathogenesis of smallpox and analogous phenomena to such effect that a convincing story is presented of the events following infection in man, although admittedly some parts of the story lack supporting evidence. [It will be possible only to summarize the argument here.]

The site of entry of the virus to the tissues is believed to be in the upper respiratory tract, although no primary lesion can be demonstrated histologically. The incubation period of naturally acquired smallpox is 2 or 3 days greater than that of inoculated smallpox and than that of the congenital variety acquired by the infant through the placenta. These 2 or 3 days might represent the interval which occurs between the implantation of virus on the mucosa of the respiratory tract and its spread by the lymphatics to the blood stream and internal organs. On the basis of absence of infectivity during the few days following infection the primary site of multiplication of the virus may be low down in the respiratory tract, for example, in the smaller bronchi or bronchioles. On the analogy of Fenner's work on mousepox (*Lancet*, 1948, **2**, 915) a primary transient viraemia is postulated which is rapidly cleared by the phagocytic cells lining the sinusoids of the liver and the sinuses in the spleen and bone marrow, and perhaps by phagocytic cells in the lung capillaries. After a further period of multiplication and progressive infection of these cells, overflow of virus takes place into the blood stream with liberation also of products of cell breakdown. This secondary viraemia marks the end of the incubation period and the onset of symptoms.

The skin and other tissues then become infected with the virus, the lesions in the skin occurring particularly at pressure points where capillary stasis may be a factor in localization. The secondary viraemia, except in severe cases, may be limited to a day or two, or even to a few hours. Of 7 patients whose blood was investigated for virus during the first 7 days of illness, positive results were obtained only up to the fifth day and, with one exception, only in those who ultimately died of the disease. Infectivity probably commences from the moment of breaking down of lesions in the mouth and pharynx with discharge of virus about the third day of the disease. When macules appear in the skin, very numerous virus particles can be detected in the stained smears from scrapings. " There must be a tremendous amount of virus in the skin of the patient who is to develop a confluent rash ".

The fall of temperature and improvement in the patient's condition from the fourth to the sixth day of illness suggests the development of immunity to the virus or its products about this time. This is also suggested by the failure of vaccination after the first or second day of the focal eruption. In actual fact antibody, as estimated by complement fixation and antihaemagglutinin, appears between the second and fifth days and increases up to the ninth day of illness. Neutralizing antibody also appears about this time but is more variable. The speed of the immune response determines the severity of the disease, and the outcome is decided by what happens in the body in the first few days of illness. In the *sine eruptione* cases antibody probably combines with the liberated virus and prevents the infection of the epithelium. If the response is less effective, some of the virus in the blood stream early in the disease may be neutralized leaving correspondingly less to infect the skin; or the antibody may prevent the progressive infection of the epithelium, so modifying the rash. The maturation of the eruption proceeds after the antibody has appeared and is dependent upon the degree of destruction of cells infected in the first few days of illness. Patients who die in the later, pustular, stage of the eruption may have a high titre of antibody, and death is due to the late effects of earlier virus activity in cases where the effect of some serious complication

and of secondary infection can be excluded. Antibody persists at a high level for some years after smallpox. After vaccination neutralizing antibody may be detectable for many years, but is not usually present in as high a concentration as after smallpox and it varies considerably in different individuals. The quality (avidity) as well as the quantity of antibody in the blood may be of importance in determining relative immunity to smallpox infection, but no experimental confirmation of this has yet been obtained. *H. Stanley Banks*

367. **The Neutralization of French Neurotropic Yellow Fever Virus by Sera of Bwamba Children**
G. W. A. DICK. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **44**, 319–328, Dec., 1950. 2 figs., 14 refs.

In 1941, following an epidemic of yellow fever thought to be carried by *Aëdes simpsoni*, the entire population of Bwamba County, Uganda, was vaccinated with 17D vaccine. Post-vaccinal surveys carried out 2 and 3 years afterwards showed that over 90% of the population had yellow-fever antibodies in the blood.

In 1946–7 studies were undertaken to determine the presence of serum antibodies in children born since the campaign. The local chiefs, who were paid 20 cents per child, brought the children to central points and the sera were tested at Entebbe by means of the 1% virus test. All sera giving inconclusive results were retested: 776 children from 16 areas were examined and 39·8% of those estimated to have been born during the period 1942 to 1945 had yellow-fever antibodies as a result of natural infections, while no less than 83·5% of those aged 5 years or over showed antibodies, presumably partly as a result of vaccination and partly as a result of the natural infection. The incidence of positives increased with each year of life, there being only 2 in 94 children of one year of age or under: thus inheritance played no part. It is considered that the antibodies are not heat-labile non-specific substances.

It is noted that the chance of infection in Bwamba increases with residence in close proximity to the forest, and it would appear that yellow fever is being introduced into the human population from this source. The difficulty is stressed of understanding how virus activity is maintained among a monkey population which is 61% immune, and a human population which is over 90% immune, without the intervention of some source of the virus other than the monkey. *R. R. Willcox*

368. **Experiments to Test the Possibility of Trans-ovarial Transmission of Yellow Fever Virus in the Mosquito *Aëdes* (*Stegomyia*) *africanus* Theobald**
J. D. GILLETT, R. W. ROSS, G. W. A. DICK, A. J. HADDOW, and L. E. HEWITT. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **44**, 342–350, Dec., 1950. 22 refs.

In the experiments described 246 wild-caught adult female *Aëdes africanus* were isolated in separate tubes and fed on 3 rhesus monkeys in the region of the lateral end of the inguinal ligament, the animals having been inoculated a few days before with a strain of yellow-fever virus recently isolated in Bwamba, Uganda. Of these mosquitoes 108 laid 164 separate batches of fertile eggs, and these egg batches were isolated and reared through to the F_1 generation of adults. The parent insects at death were triturated individually and inoculated intracerebrally into mice to test for the virus, which was shown to be present in 36 of the parents. The F_1 adults were kept individually for a minimum of 18 days and then inoculated into mice in the same way as their mothers. Altogether 1,892 F_1 adults were produced, 610 of them from known infected parents, but yellow-fever virus was recovered from none. *R. R. Willcox*

369. **The Cyclical Transmission of Yellow Fever Virus through the Grivet Monkey, *Cercopithecus aethiops centralis* Neumann, and the Mosquito *Aëdes* (*Stegomyia*) *africanus* Theobald**
R. W. ROSS and J. D. GILLETT. *Annals of Tropical Medicine and Parasitology* [*Ann. trop. Med. Parasit.*] **44**, 351–356, Dec., 1950. 1 fig., 14 refs.

Experiments were conducted to ascertain whether yellow-fever virus could be maintained in the monkey solely by cyclical transmission through *Aëdes africanus*, a method which is believed to occur naturally in Bwamba, Uganda. Two series were initiated by injecting rehydrated dried serum containing yellow-fever virus into rhesus monkeys obtained from India, the inoculum being titrated into mice. Cultured *A. aegypti* were allowed to feed on the monkeys 4 days after inoculation, each monkey being bled daily and the serum titrated in mice. After the mosquitoes had been kept for 18 to 19 days they were allowed to engorge on fresh, non-immune rhesus monkeys.

In the first series *A. aegypti*, and in the second *A. africanus*, were fed on the third, fourth, and fifth days. Those feeding when the titre was shown to be high were kept for 39 and 23 days respectively, and then were allowed to feed on grivet monkeys obtained from the region of Lake Victoria. *A. africanus* were then fed on these monkeys and the two series of cyclical transmissions employing grivet monkeys and *A. africanus* only were begun. In the first series two complete cycles involving 3 grivet monkeys were achieved with wild *A. africanus* caught on the skin as they prepared to bite. In the second series three complete cycles involving 4 grivet monkeys were achieved with laboratory-bred *A. africanus*. As three abortive attempts were made before the main series was begun it is considered that a high titre of the virus is necessary for transfer. *R. R. Willcox*

370. **Poliomyelitis and Diphtheria Immunization in Belfast**
W. J. MCLEOD. *British Medical Journal* [*Brit. med. J.*] **1**, 736–738, April 7, 1951. 5 refs.

The experience of Belfast on the relation of diphtheria immunization to the poliomyelitis epidemic of 1950 is discussed. A total of 98 cases of poliomyelitis were reported up to Sept. 19, of which 10 were non-paralytic. The incidence under 5 years was 13 per 10,000 of the population in this age group. The epidemic wave gradually rose from the middle of March to a peak in

the middle of July. Immunization against diphtheria continued as usual until the holiday closure of the clinics on July 8. Administrative action was taken in Northern Ireland late in July to discourage immunization during the epidemic. [It would seem, although not precisely stated, that combined diphtheria–pertussis inoculation was almost entirely suspended during the epidemic.] It is estimated that some 2,000 inoculations of A.P.T. were given by general practitioners during the epidemic [presumably nearly all before the end of July, that is, during the first half of the epidemic]. In this group one " double event " occurred—inoculation into the right hip followed 8 days later by paralysis of the right leg. In addition there was one case of facial paralysis following 23 days after P.T.A.P. inoculation in the left arm.

The suggestion is made that subcutaneous P.T.A.P. inoculation, which produces less local reaction than A.P.T., is a relatively innocuous antigen so far as induction of poliomyelitis in the inoculated limb is concerned. This is based on the complete absence of association between the site of inoculation and the site of paralysis after 6,250 inoculations of P.T.A.P. performed in the clinics " during the epidemic ". [From the text it would seem, however, that these inoculations were given during the period Jan. 1 to July 8. From January to the middle of April there were very few cases of poliomyelitis, and from the middle of April until July 8 presumably no more than one-half of the total number. The negative experience of " double events " with P.T.A.P. is therefore not so favourable as it is represented to be in the discussion and summary of this paper. In this respect the article seems to the abstracter to be somewhat misleading.] *H. Stanley Banks*

See also Section Endocrine Disorders, Abstract 277.

371. **Changes in Water Metabolism in Acute Infective Hepatitis.** (Изменения водного обмена при остром инфекционном гепатите)

L. N. GOLDMAN. Терапевтический Архив [*Terap. Arkh.*] **22**, No. 6, 56–60, 1950. 3 refs.

The role of the liver in the water metabolism of the body is little understood. It is probably not purely mechanical, but involves also a hormonal influence similar to that of the endocrine glands.

In 52 cases of parenchymatous hepatitis it was found that during the stage of onset there was a severe fall in the alkali reserve, in one case to 20 ml., and considerable retention of water in the organism, up to 2,400 ml. Folgard's test showed a percentage of water excretion varying from 56 to 89 in 4½ hours. McClure's test showed an acceleration of blister formation, pointing to retention of water in the tissues. These findings were reversed in the stage of remission.

With intense jaundice urinary excretion was much reduced during movement compared with that during rest. This phenomenon also largely disappeared after recovery, which suggests that a circulatory factor is at least partly responsible for fluid retention.

Mercurial diuretics, such as " merkusal ", produced an intense diuresis in the early stage of hepatitis—from 3 to 4 litres. *L. Firman-Edwards*

372. **Japanese B Encephalitis in Korea. The Epidemic of 1949**

R. L. HULLINGHORST, K. F. BURNS, YOUNG TAI CHOI, and L. R. WHATLEY. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **145**, 460–466, Feb. 17, 1951. 3 figs., 28 refs.

From the Bureau of Preventive Medicine, Seoul, Korea, the authors describe an epidemic of encephalitis which occurred in Korea during the summer of 1949. The outbreak was shown to be due to the virus of Japanese B encephalitis. Between August and October, 1949, 5,545 cases were reported, with 2,429 deaths. Histological investigation revealed the diffuse, non-purulent encephalitis characteristic of Japanese-B type of infection. This conclusion was supported by serological tests and by the recovery of a neurotropic virus from the brain in a fatal case. Serum from normal Koreans and from healthy animals subjected to anamnestic evaluation demonstrated a widespread dissemination of the virus throughout Korea. *Joseph Ellison*

373. **Critical Evaluation of Antihistaminic Drugs in the Common Cold**

N. D. FABRICANT. *Archives of Otolaryngology* [*Arch. Otolaryng., Chicago*] **52**, 888–899, Dec., 1950. 22 refs.

" As the result of extravagent and irresponsible claims in behalf of antihistamine drugs, the American public has been deluded into spending huge sums of money on the ' sensational new discovery that kills colds in hours '. It will continue to do so until it is educated by alert physicians to the foolishness of such practice." The author amplifies these remarks with a list of dangerous complications produced by the antihistamine drugs in patients taking them for the common cold: 3 cases of haemolytic anaemia, 3 of agranulocytosis, rashes, cardiac excitation, headache, tinnitus, fever, as well as the better known effects such as drowsiness and dizziness. In a survey by 247 physicians 223 reported having noted side-effects of antihistamine drugs in their patients.

There is no real evidence that allergy is mainly responsible for the common cold. Most of the writers who advocated these drugs for the common cold failed to differentiate between the infective cold and vasomotor disturbances or allergic conditions. Fully controlled studies in the United States and in Great Britain have demonstrated the failure of antihistaminics in the treatment and control of the genuine " common cold ". To these studies is now added a carefully controlled research on 213 students. It is concluded that " antihistaminic drugs do not prevent, abort, shorten, curtail, reduce, or stop the common cold. It was observed that antihistaminic drugs are no more effective than placebos in aborting a cold and that there is no validity to the contention that antihistaminic drugs are more effective if taken within a short time after the start of a cold ". *F. W. Watkyn-Thomas*

374. **Herpangina. Etiological Studies of a Specific Infectious Disease**
R. J. HUEBNER, R. M. COLE, E. A. BEEMAN, J. A. BELL, and J. H. PEERS. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **145**, 628–633, March 3, 1951. 1 fig., 11 refs.

In a Maryland community under epidemiological surveillance, similar mild illnesses occurred in rapid succession among 6 children in the summer of 1950. The attacks were sudden and of short duration, with fever, slight sore throat, headache, and abdominal pain. The throat lesions were characteristic, with petechiae mainly on the anterior pillars of the fauces, becoming papular surmounted by small vesicles which developed into punched-out ulcers. There had been close contact between the patients. The illness resembled herpangina, a previously described clinical entity thought to be caused by herpes simplex virus. Extensive investigation failed to isolate herpes simplex virus or other known pathogens from the throats of the patients, but a strain of Coxsackie virus, H3, was obtained from the stools of the 6 patients and from the throats of 3. High levels of neutralizing antibody were present in convalescent serum from 4 patients. As this phenomenon was not demonstrated with other viruses, infection was considered to be specific. No Coxsackie virus was isolated in a community survey before the outbreak, but the H3 strain was obtained from a further 12 contacts, only one of whom gave a history of herpangina, in a post-infection survey.

It was found on further investigation that similar illnesses were prevalent in the Washington area. From these, four distinct strains of Coxsackie virus were recovered, two having been previously isolated in 1949. These strains differed also from Dalldorf's group A, Types 1, 2, and 3, and from Melnicks's High Point strains. It was not found possible to recover Coxsackie virus from the blood, nor was herpes simplex virus isolated from the throat lesions of 8 patients investigated.

Typically this was a summer disease, with infection mainly in children under 5 and multiple cases in a household, suggesting person-to-person transmission. The incubation period was 3 to 5 days, with a range of 2 to 9 days. The association between virus and infection appeared significant as it rarely occurred in persons not in recent contact with known cases. It is suggested that herpangina may be the chief clinical manifestation of human infection with many strains of Coxsackie virus.

Support is given to the name herpangina despite the misleading inference that it is caused by herpes simplex virus. *A. D. Macrea*

375. **Orf in London**
I. S. HODGSON-JONES. *British Medical Journal* [*Brit. med. J.*] **1**, 795–796, April 14, 1951. 2 figs., 8 refs.

A series is described of 8 human cases of orf, a form of dermatitis due to a specific virus which occurs in sheep. This disease, though by now well known in sheep-rearing districts, has hitherto seldom been recognized in southern England or in London. Of the 8 patients, 6 were meat porters at Smithfield, one a London butcher, and one a housewife who had handled sheeps' heads 14 days before the lesions appeared. Orf is a self-limiting disease, the course of which is 5 to 8 weeks: no specific treatment is at present known. The importance of recognizing orf lies in differentiating it from pyococcal infections in which surgery and antibiotics may be usefully employed.

Photographs of lesions in 2 cases are reproduced.
Joseph Ellison

TUBERCULOSIS

376. **Agranulocytosis due to Treatment with Thiacetazone (TB I).** (Agranulocytose etter TB I-behandling)
T. KAHRS. *Tidsskrift for den Norske Lægeforening* [*Tidsskr. norske Lægeforen.*] **71**, 143–145, March 1, 1951. 3 figs., 3 refs.

A fatal complication of thiacetazone treatment is described. A 58-year-old gardener was admitted to Ullevål Hospital, Oslo, with extensive bilateral tuberculosis with cavitation. The sputum contained acid-fast organisms. After 2 months' treatment, during which he received 12·7 g. of thiacetazone, he became febrile and developed acute exfoliative dermatitis. The drug was promptly withdrawn, the patient improved, and the rash subsided. Three weeks later he again became febrile and examination of the blood then showed that the haemoglobin level, hitherto normal, was now 50% and the leucocyte count was 2,200 per c.mm. The clinical condition was one of agranulocytosis, from which the patient died 6 days later. Necropsy showed chronic fibroid tuberculosis with bronchiectasis and emphysema. The liver had undergone fatty degeneration, and in the bone marrow atrophy of the myeloid tissue with replacement by fat cells was found. *J. E. M. Whitehead*

377. **The Domiciliary Use of Paramisan Sodium in the Treatment of Pulmonary Tuberculosis**
D. L. PUGH, E. R. JONES, and W. J. MARTIN. *Tubercle* [*Tubercle, Lond.*] **32**, 50–58, March, 1951. 1 fig., 3 refs.

A series of 50 patients with pulmonary tuberculosis were treated by the authors with sodium *p*-aminosalicylate (PAS) and their progress compared with that of 106 controls. [The dosage given is not reported.] The course of treatment lasted 12 weeks and the condition of each patient was assessed at the start of treatment and 12 weeks after its completion by considering the radiological appearances, weight, erythrocyte sedimentation rate, toxaemia [this is not defined], and examination of sputum for tubercle bacilli. Few complications were noted; one patient is stated to have shown evidence of acquired idiosyncrasy, but this is not described; digestive disturbance occurred in 26 cases. In 5 cases tubercle bacilli in the sputum became resistant to a concentration of 6·4 mg. of PAS per 100 ml. of medium.

The authors' assessment shows that in treated cases greater progress was made towards healing of tuberculous lesions than in the untreated cases. PAS is extremely useful in preparing patients for collapse therapy and may be of greater value than pneumoperitoneum in

"cooling off" active lesions before artificial pneumothorax. It is not a panacea, but has a place in a planned, combined attack on the disease. *L. M. Franklin*

378. **Peroral B.C.G. Vaccination.** (Peroral BCG-vaksinasjon)
H. J. USTVEDT. *Tidsskrift for den Norske Lægeforening* [*Tidsskr. norske Lægeforen.*] **71**, 135–137, March 1, 1951. 2 refs.

There has recently been a revival of interest in the peroral method of B.C.G. vaccination following the work of de Assis, in Brazil, who administers 200 mg. of vaccine by mouth followed by 100 mg. monthly for 3 to 5 months. Among the advantages claimed for this method are that tuberculin-positive individuals can be vaccinated without harm, ease of administration, a high conversion rate, and a high degree of protection. A small investigation of the peroral method was made at Ullevål Hospital, Oslo. Owing to the difficulty of finding tuberculin-negative, unvaccinated individuals in Norway the numbers available were small. The vaccine, in a single dose of 200 mg., was given to 20 chronic sick patients with both strong and weak sensitivity to tuberculin, without ill-effect; 10 came to necropsy from 7 days to 4 months later, but no changes ascribable to the vaccine could be found. In 50 healthy individuals, some tuberculin-negative or weakly positive, to whom the vaccine was given there were no symptoms or signs ascribable to vaccination, and in 6 who were *x*-rayed 7 months afterwards there were no signs of calcified abdominal glands. Of 8 tuberculin-negative nurses who were vaccinated with 200 mg. by mouth, all but 2 were tuberculin-positive one month later, when they were revaccinated with 100 mg. orally. All were positive one month later, and 7 were still positive 7 months later. Out of a group of 6 nurses given a single dose of 200 mg. orally, 5 were tuberculin-positive 3 months later. Peroral vaccination had little effect on the tuberculin sensitivity of 10 individuals who had been vaccinated 2 to 6 times previously by the intracutaneous method without becoming positive. The de Assis method requires further investigation with regard to possible ill-effects and ability to produce permanent sensitivity to tuberculin. *J. E. M. Whitehead*

379. **Research Contributions of BCG Vaccination Programs. I. Tuberculin Allergy as a Family Trait**
C. E. PALMER and S. N. MEYER. *Public Health Reports* [*Publ. Hlth Rep., Wash.*] **66**, 259–276, March 2, 1951.

380. **Disturbances of Intestinal Function and Morphological Changes in the Vegetative Nervous System in Tuberculosis.** (О нарушениях функции кишечника и морфологических изменениях вегетативных нервных приборов его при туберкулезе)
S. S. VAIL and L. P. PROTAS. Архив Патологии [*Arkh. Patol.*] **12**, No. 6, 4–15, 1950. 8 figs., 13 refs.

Previous work by Soviet authors had demonstrated that the nerve cells of the intramural plexuses of the gastro-intestinal tract are frequently affected in tuberculosis, showing degenerative changes even in the absence of mucosal involvement. In the present series 12 cases were studied radiologically and this was followed by a histological study of the intestine, obtained either by resection at operation or after death. A correlation was found to exist between the degree of nerve-cell involvement and the disturbances of function (observed radiologically) such as irregularities of intestinal tone and mobility. There was, on the other hand, no direct correlation between the degree of nervous involvement and the number of tubercles and ulcers in the mucosa. *L. Crome*

381. **Clinical Study of Tuberculosis of the Caecum not associated with Pulmonary Disease.** (К клинике туберкулезного тифлита (не осложненного легочным процессом))
N. A. SHMELEV and E. F. ADNOLETKOVA. Клиническая Медицина [*Klin. Med., Mosk.*] No. 1, 26–32, 1951. 25 refs.

The authors describe in detail the anatomy of the ileo-caecal valve and caecum and explain why this region, together with the terminal part of the ileum, is often the site of tuberculous disease. They describe the findings in 30 cases of tuberculosis of the ileo-caecal region, in which pulmonary tuberculosis was either absent or inactive and in which no case of tuberculous peritonitis or lymphangitis was found. They consider that tuberculosis of the caecum may be the primary focus of tuberculosis, resulting from the swallowing of the bacilli. Many of their patients had been in close contact with sufferers from a pulmonary infection. Tuberculosis of this region is usually a chronic disease, but sometimes has an acute onset and rapid course: 22 of the patients gave a history of over 2 years, and 7 of them of over 5 years, while one of these had had the disease for 26 years. In the commoner chronic type progress of the disease was "wave-like", as in many other forms of chronic tuberculosis.

Two types are described—the ulcerative and the hyperplastic. The diagnosis is made mainly on clinical grounds; radiological evidence is valuable, but laboratory findings play a minor role, since the isolation of tubercle bacilli from the stools is difficult owing to their bulk and in any case is possible only if ulceration has occurred. In addition to the general signs of infection there is a tendency to constipation and abdominal pain. On palpation, the thickened walls of the bowel can be felt. Radiological screening after a barium enema reveals defects in contour and filling, accumulation of barium in the terminal ileum, and tenderness over this area. [The erythrocyte sedimentation rate appears to have been normal in the cases described in detail.] In acute cases early diagnosis is seldom easy; in 2 of the authors' cases the first diagnosis was typhoid fever, and in one "acute abdomen"; in the latter, laparotomy revealed the true state of affairs.

Differential diagnosis must take into consideration not only the above conditions, but also appendicitis, chronic colitis, terminal ileitis, mesenteric lymphangitis, non-specific lymphadenitis, and new growth. In difficult cases subcutaneous injection of tuberculin, cautiously

raised to a dosage which will evince a mild focal reaction, is of great assistance. In the absence of pulmonary disease the finding of tubercle bacilli in the stools is strong evidence that an ileo-caecal lesion is tuberculous. Usually, however, the diagnosis must rest on the clinical and radiological findings.

Treatment consists of rest, diet (nourishing and varied, but not over-abundant), and warmth. Tuberculin and streptomycin play a valuable part, the latter being best when administered intraperitoneally. Resection should be reserved for cases with obstruction from tumour formation.

[The authors appear to underestimate the importance and frequency of terminal ileitis, and the difficulty of excluding it in the absence of clear bacteriological evidence of tuberculosis.] *L. Firman-Edwards*

382. **Pathology of Tuberculosis Treated with Streptomycin: a Review of 34 Cases**
O. AUERBACH, L. WEISS, and G. N. STEMMERMANN. *Diseases of the Chest* [*Dis. Chest*] **19**, 145–157, Feb., 1951. 7 refs.

The literature on the findings at necropsy in cases of tuberculosis treated with streptomycin is reviewed. It indicates that although there are no specific pathological changes peculiar to streptomycin therapy, the time of healing appears to be shortened. Perifocal reaction is diminished, with consequent diminution in the ultimate amount of fibrosis, and lesions on superficial surfaces show more healing than those in solid organs. No correlation between findings and the sensitivity of the organism is reported.

The authors review their necropsy findings in 33 cases of chronic pulmonary tuberculosis and one of tuberculous meningitis, in all of which streptomycin had been given. They divide them into three groups according to the sensitivity of the organism at the time of death: (1) 7 cases in which the organism was still sensitive and in which there were the beneficial changes attributed to streptomycin therapy, including increased hyalinization in the walls of the pulmonary cavities; (2) 20 cases in which resistance had developed, in which there was wide perifocal reaction, with little healing of recent foci and the development of tuberculous ulcers in the upper respiratory and gastro-intestinal tracts; (3) 7 cases where the details of resistance were inadequate, though in several cases necropsy suggested that the organism was still sensitive.

In 4 cases of chronic pulmonary tuberculosis with tuberculous meningitis thick caseous masses at the base of the brain were surrounded by dense layers of hyalinized connective tissue, in contrast to the findings in untreated cases. *A. Ackroyd*

383. **The Delay in the Diagnosis of Tuberculous Meningitis and its Relation to the Results of Treatment**
J. LORBER. *Proceedings of the Royal Society of Medicine* [*Proc. roy. Soc. Med.*] **44**, 1–3, Jan., 1951.

Figures showing the results of streptomycin treatment of tuberculous meningitis in the Department of Child Health, University of Sheffield, give convincing proof that streptomycin is an effective weapon against the disease. In 54 cases the total over-all mortality was 51·8%, 26 survivors being followed up for an average of 16·3 months from the beginning of treatment. This mortality was reduced to 14·2% if all cases of delay in beginning streptomycin were eliminated: only 2 deaths occurred in 14 children who developed meningitis while already under observation or under treatment for primary or miliary tuberculosis and where there was no measurable delay. In 23 cases where treatment was begun on or before the 14th day of illness the mortality was 47·8%; in 17 cases where treatment was begun on or after the 15th day the mortality was 88·2%.

There appears to be no doubt of the consequences of delay; the duration of delay was: (1) between the onset of symptoms and the doctor's first call, average 3·3 days; (2) between the doctor's first call and the child's admission to hospital, average 8·3 days; (3) transfer from other hospitals, average 2·4 days (3 days in 1948, reduced to 1·4 days in 1950); (4) between admission and the beginning of treatment, average 1·2 days, range 0 to 5 days. The average total delay was 14·2 days; the generally accepted average duration of the untreated disease to death is 21 days. Thus two-thirds of the course of the disease proceeded without therapy, placing the form of treatment at a great disadvantage.

The author states that the first need in achieving earlier diagnosis and treatment is an efficient tuberculosis service. Children with a positive tuberculin skin reaction should be carefully supervised, frequently examined, and always considered to have had a fresh infection. The significance of the findings should be impressed upon both the parents and the family doctor. The longest delay occurred after the family doctor had been consulted, and here there was no improvement from 1948 to 1950. The tuberculin jelly test, which is neglected, is valuable and is one of the simplest. Tuberculosis is common enough to kill 2,000 children in England every year. On admission to hospital of a child suspected of having meningitis, lumbar puncture should be carried out immediately, together with a radiograph of the chest, a tuberculin skin test, and examination of the fundi for choroidal tubercles.
John Sumner

384. **Tuberculous Meningitis. Results of Treatment with Streptomycin and Intrathecal Sulphetrone**
W. L. CALNAN, J. RUBIE, and A. F. MOHUN. *British Medical Journal* [*Brit. med. J.*] **1**, 792–793, April 14, 1951. 1 fig., 6 refs.

The authors divided 48 consecutive cases of tuberculous meningitis, including 9 with miliary tuberculosis in addition, into two groups of 24, each group containing approximately the same number of early, medium, and advanced cases and including children of under 3 years and over 3 years. One group was treated with streptomycin in a daily dose of 0·02 g. per lb. (0·044 g. per kg.) body weight intramuscularly and 0·1 g. in 10 ml. saline intrathecally. The other group, in addition to this treatment, had 200 mg. solapsone (" sulphetrone ") intrathecally daily, mixed with the streptomycin. Toxic effects seen were convulsions (5 cases), excessive

head retraction and opisthotonos (7 cases), mental symptoms (3 cases), and cyanosis (1 case). In 5 cases these were severe enough to necessitate interruption of treatment. The results after a minimum of 12 months' observation showed 14 (58%) survivors in each group and, in common with the authors' clinical impressions, give no indication that sulphetrone injected intrathecally is a valuable addition to streptomycin treatment of tuberculous meningitis. *H. Stanley Banks*

See also Sections Pharmacology and Therapeutics, Abstracts 73–4; Radiology, Abstract 112.

OTHER BACTERIAL INFECTIONS

385. **Thiosemicarbazone (TB-I) in the Treatment of Leprosy. Preliminary Communication**
M. VEGAS, J. CONVIT, J. A. MEDINA, and E. DE BLOMENFIELD. *International Journal of Leprosy* [*Int. J. Leprosy*] **18**, 451–455, Oct.–Dec., 1950. 2 refs.

As a result of a visit by Domagk to Venezuela in 1949, thiacetazone (" TB I " or "conteben"), of reputed value in tuberculosis, was tried in 42 lepromatous cases, of varying degrees of severity, at the Cabo Blanco Leprosarium. The initial results were quite favourable; in 21 cases there was marked regression of lesions at the end of 6 months' treatment with a daily dosage varying from 100 to 900 mg. of the drug. *R. Wien*

386. **The Sulfone Treatment of Tuberculoid Leprosy**
J. LOWE. *International Journal of Leprosy* [*Int. J. Leprosy*] **18**, 457–468, Oct.–Dec., 1950. 20 refs.

The use of the sulphones in leprosy has hitherto been confined to the treatment of lepromatous cases. This restricted use seemed illogical to the author and he accordingly treated more than 50 tuberculoid cases with solapsone and diaminodiphenylsulphone. All the cases responded to treatment; usually within 6 months the lesions became inactive, showing only varying degrees of atrophic wrinkling with loss of pigment and of cutaneous sensibility. The sulphone drugs thus appear to be of value in tuberculoid as well as lepromatous cases. *R. Wien*

387. **A Note on 40 Cases of Typhoid or Paratyphoid Fever in Infants Treated and Cured with Chloramphenicol.** (Note sur 40 cas de fièvre typhoïde ou paratyphoïde de l'enfant traités et guéris par la chloromycétine)
J. MARIE, P. SERINGE, G. SEE, and P. MARLAND. *Semaine des Hôpitaux de Paris* [*Sem. Hôp. Paris*] **27**, 630–635, Feb. 26, 1951. 4 figs., 17 refs.

Although typhoid fever usually runs a benign course in infants, the mortality before the days of modern antibiotics was not negligible. The authors treated 40 cases of typhoid or paratyphoid B between September, 1949, and September, 1950, with chloramphenicol. All these patients recovered rapidly. Convalescence was established always within a week and generally in 4 days. No complications occurred after the inception of treatment, but 2 cases of typhoid encephalitis and one of typhoid osteomyelitis were cured completely when the antibiotic was employed. Only one patient suffered relapse, the symptoms returning twice, with positive blood cultures, after apyrexial intervals of a fortnight; both relapses responded rapidly to renewed chemotherapy. It is suggested that these episodes were due to the release of organisms from the gall-bladder where they had been shielded from the impact of the antibiotic. On the second occasion an attempt at medical drainage was made with posterior pituitary extract and adrenaline. Small infants received 50 to 100 mg. per kg. body weight, and larger infants 1·5 to 2 g. of chloramphenicol daily by mouth. No difficulty was found in getting the capsules swallowed. They were softened in boiled water and then placed on the tongue immediately before the presentation of a feed. The authors deprecate the use of a " loading dose " and, indeed, recommend the use of half-doses for the first 2 days of treatment. It is to this routine that they attribute the freedom from side-effects in their series. The chemotherapy must be maintained for an adequate period, which is considered to be between 1 and 2 weeks. No evidence was found to support the suggestion that the use of chloramphenicol interferes with the proper development of antibodies to the infection. *T. A. A. Hunter*

388. **The Morbid Anatomy of the Liver in Diphtheria.** (Il quadro anatomo-patologico del fegato nella difterite)
B. GARAU. *Annali Italiani di Pediatria* [*Ann. ital. Pediat.*] **3**, 517–530, Dec., 1950. 6 figs., 19 refs.

The macroscopical and microscopical findings in the liver are reported in 29 cases of diphtheria occurring in children between the ages of 2½ months and 4 years. In almost every case the duration of the disease was 17 days or less.

The liver was found to be slightly enlarged and congested, and although its consistency suggested an increased fibrous-tissue content, this was not borne out by the subsequent histological examination. The microscopic lesions consisted of scattered foci of degeneration and necrosis, together with cellular collections composed of lymphocytes and monocytes with occasional polymorphonuclear leucocytes. These collections were often seen around the portal tracts and subcapsularly. Foci of fatty change were present in addition to centrilobular congestion.

The histological picture is that which might be seen in any severe infection and possesses no specific characteristics. *G. J. Cunningham*

389. **Treatment of *Hemophilus influenzae* Meningitis with Chloramphenicol and Other Antibiotics**
F. R. MCCRUMB, H. E. HALL, J. IMBURG, A. MERIDETH, R. HELMHOLD, J. BASORA Y DEFILLO, and T. E. WOODWARD. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **145**, 469–474, Feb. 17, 1951. 4 figs., 12 refs.

The effect of chloramphenicol alone in the treatment of 12 cases of *Haemophilus influenzae* meningitis occurring in children whose ages ranged from 5 months to

5 years (mean 2·4 years.) is described. Experiments on mice demonstrated that while streptomycin, aureomycin, and chloramphenicol varied but slightly in protective power, terramycin was inferior and penicillin ineffective against *H. influenzae*. Chloramphenicol was chosen for use because of ease in administration, low toxicity, and a stability which simplified bio-assay.

In the present series chloramphenicol was given orally, with an initial dose of 750 mg. followed by 250 mg. 4-hourly. The average duration of fever after instituting therapy was 2·3 days. There was rapid improvement, with return of consciousness, in an average of 1·3 days. All patients recovered and in one only was there any neurological residue—a patient in whom treatment had begun only on the seventh day, after terramycin had failed. In 5 cases the concentration of chloramphenicol in the cerebrospinal fluid averaged 13·2 μg. per 100 ml., roughly half that in the blood.

The authors state that they have insufficient facts on which to recommend an optimum concentration, but with the dosage here employed no toxic manifestations were encountered. Oral administration presented no serious difficulty, but it is stated that rectal administration of 500 mg. aids in the oral treatment. The mean duration of treatment was 8 days and the total received by one patient 10·4 g. The authors express the opinion that at present chloramphenicol is the antibiotic best suited to deal with infection by any of the Gram-negative group of pathogens.

Joseph Ellison

390. **Modification of Whooping-cough in Contacts by means of Chloramphenicol**
A. BOGDAN. *Lancet* [*Lancet*] **1**, 764–766, April 7, 1951. 5 refs.

A study is presented of the treatment of contacts of known cases of whooping-cough, in the preparoxysmal stage, with chloramphenicol. The dosage given was 10 mg. chloramphenicol per lb. (22 mg. per kg.) body weight per day given in 5 doses mixed with milk or jam for 5 days. In addition symptomatic treatment was given to all patients. In 10 out of 13 contacts the chloramphenicol successfully modified the illness. These results apparently did not depend on whether *Haemophilus pertussis* was cultured from prenasal or postnasal swabs or not. Four cases are reported in detail. The protection given appears to be immediate.

It is doubtful whether such cases are followed by immunity.

Margaretha Adams

391. **Chloramphenicol in the Treatment of Pertussis. Review of a Hundred Cases**
H. C. A. LASSEN and L. C. GRANDJEAN. *Lancet* [*Lancet*] **1**, 763–764, April 7, 1951. 1 fig., 4 refs.

At the Department of Epidemiology of the University of Copenhagen the authors treated 100 patients with typical whooping-cough with chloramphenicol for 3 to 5 days in the first 2 to 3 weeks of the illness.

In 93 cases the chloramphenicol was administered rectally in suppositories (0·5 g. to 1 g.+4×0·25 g. to 5 g. on first day, followed by 5×0·25 to 0·5 g. on the next 4 days), whereas 7 older children and adults took it in capsules by mouth (1·5 g. to 3 g.+4×0·75 g. to 1·5 g. on first day, followed by 5×0·75 g. to 1·5 g. on the next 5 days). Swab cultures of the nasopharynx were examined every other day. Of the 80 patients with positive cultures before treatment 73 became negative within 9 days of chloramphenicol being started. *In vitro* investigations showed that the few therapeutic failures were not related to the occurrence of resistant strains. As a rule the nasopharynx became free from infection in 48 hours from the start of a course of chloramphenicol. The general condition improved considerably after a few days' treatment. The frequency of the paroxysms fell sharply after 3 to 5 days' treatment.

Minor side-effects appeared in 14 cases: 7 children had perianal dermatitis, 4 had slight diarrhoea, 2 who took chloramphenicol orally had occasional vomiting, and one developed a general erythema.

Margaretha Adams

392. **Fulminating Sonne Dysentery in Children**
I. C. LEWIS and A. E. CLAIREAUX. *Lancet* [*Lancet*] **1**, 769–771, April 7, 1951. 8 refs.

The authors describe the occurrence in an Edinburgh hospital during 1935–50 of 16 cases of fulminating dysentery due to *Shigella sonnei*. In 15 of these cases convulsions preceded admission to hospital. Other symptoms were vomiting, loose stools, anorexia, headache, fever, and abdominal pain. Loose stools or mucus were passed within 24 hours of admission to hospital, but blood was noted in stools from 3 patients only. Five patients died, the average time between onset and death being 22 hours; of these 5, 3 were infants of between 18 months and 2 years and the other 2 were aged 2½ and 4 years. True dysenteric ulceration was found in two of the fatal cases, whereas in the other 3 only slight pathological changes were observed.

The best method of isolating *Sh. sonnei* after necropsy was found to be by incubating a section of the infected bowel in selenite broth for 24 hours at 37° C. and then subculturing on triple-S-agar

Detailed histories of the 16 cases of Sonne dysentery are given.

R. A. Neal

393. **Chloramphenicol and the Combination of Chloramphenicol and Immune Therapy in Treatment of Brucellosis.**
(Il cloramfenicolo e l'associazione cloramfenicolo-immuno-terapia nel trattamento della melitense)
F. MUSOTTO and A. ROMANO. *Minerva Medica* [*Minerva med., Torino*] **42**, 177–184, Jan. 27, 1951. 3 figs., 9 refs.

There is reason to believe that infection with *Brucella melitensis* is more liable to relapse than that with *Brucella abortus* or *Brucella suis*, in spite of treatment with chloramphenicol. An account is given of the cases of 10 soldiers who contracted an infection with *Br. melitensis* through drinking raw goat's milk while serving in Sicily. In 7 the diagnosis was confirmed by positive blood culture; blood serum from the other 3 agglutinated *Br. melitensis* in high titre: 5 were treated with chloramphenicol alone, but 3 of them relapsed within 40 days; 5 new patients and the 3 with relapse were

given combined treatment with chloramphenicol and intravenous vaccine. Of these 8 patients, 6 had no relapse after 3 to 4 months, but 2 (including 1 of the 3 who relapsed after chloramphenicol alone) had a relapse after the combined treatment.

Chloramphenicol was given in the accepted dosage, though the loading dose was left out in some cases. Fever disappeared within 24 to 72 hours and treatment with the drug was continued for 5 to 7 days after this. The aggregate dose was 20 to 25 g. in each case. The vaccine was given as soon as the temperature was normal, starting with 25,000,000 organisms and further doses being given at 2- to 3-day intervals; it is now thought that 3 or 4 injections is all that is required, provided that a good pyrexial reaction is obtained, to consolidate the antibiotic action of the chemotherapeutic drug. Spleen and liver enlargement and various complications which are frequent in brucellosis improved with this combined treatment. Chloramphenicol acted equally on the patients in relapse and on those with a first attack; there was no evidence of resistance. All cases were treated within 30 days of the onset. *J. Cauchi*

394. **Terramycin, Chloramphenicol and Aureomycin in Acute Brucellosis. A Preliminary Report**
J. H. KILLOUGH, G. B. MAGILL, and R. C. SMITH. *Journal of the American Medical Association* [*J. Amer. med. Ass.*] **145**, 553–556, Feb. 24, 1951. 2 figs., 17 refs.

Of 39 male patients between the ages of 17 and 50 suffering from acute brucellosis for from 11 to 185 days before treatment, 12 were given chloramphenicol, 11 aureomycin, and 16 terramycin. Serial blood and urine cultures were made and the patients observed for up to 6 months after therapy, which consisted of 50 mg. orally of chloramphenicol or aureomycin per kg. body weight every 3 hours, or 75 mg. of terramycin orally per kg. body weight every 4 hours; this last dose was raised to 100 mg. in one case and in second courses. The drugs were administered for 7 to 14 days after the patients became afebrile, which occurred on the average in 3·4 days with terramycin, 5·1 days with chloramphenicol, and 4·8 days with aureomycin after beginning treatment; with this exception all 3 drugs were equally effective in all cases. Side-effects were: some anorexia and nausea with aureomycin; some glossitis with chloramphenicol; none with terramycin. Of the 39 cases, however, no less than 27 relapsed within 2 to 3 weeks, 9 of them giving positive cultures without any fresh clinical symptoms. Lower relapse rates reported elsewhere may have been due to failure to continue serial blood and urine cultures for some months after treatment in the absence of clinical symptoms. Further studies are being made in an effort to prevent the frequent relapses after treatment with any of these 3 drugs. *Dushanka Wolstenholme*

395. **Chemotherapy in Cholera**
S. C. LAHIRI. *British Medical Journal* [*Brit. med. J.*] **1**, 500–504, March 10, 1951. 8 refs.

Of 268 patients suffering from cholera, 72 received sulphaguanidine, 64 formosulphathiazole, and 61 formosulphacetamide; 71 were controls. The drugs were used in a dosage of 4 g. initially and 2 g. 4-hourly until symptoms subsided or stools became vibrio-free. Adjuvant treatment in the form of saline transfusions was given where necessary. *Vibrio cholerae* was found in the stools in 197 cases. In the above order, the respective mortality rates per cent. were 30.55, 34·37, 34·43, and 18·31. In severe cases the rates were 45·16, 48·75, 43·33, and 32·26 respectively. Thus the lowest rates were obtained in the control groups, results being similar in vibrio-positive and vibrio-negative groups. Peripheral circulatory failure and uraemia were the usual causes of death, the latter being most frequent in the cases treated with the formol compounds. Studies of blood concentration indicated some absorption of all drugs. None of the compounds expedited the disappearance of *V. cholerae* from the stools. It is thus obvious that these forms of chemotherapy had no beneficial effect and, in fact, may have aggravated the renal dysfunction. The most important factor in the treatment of the fully developed case is correction of water and mineral depletion. *J. L. Markson*

PROTOZOAL INFECTIONS

396. **The Histological Changes in the Brain in Cases of Cerebral Malaria.** (Гистологические изменения половного мозга при коматозной малярии)
G. A. EPREMIAN. Архив Патологии [*Arkh. Patol.*] **12**, No. 6, 19–23, 1950. 2 figs., 13 refs.

The following brain lesions were found in 22 subjects dying from cerebral malaria. Congestion and oedema of the brain were found in all of them. Ring and pinpoint haemorrhages were present in 19 cases. Vascular thrombi and infarcted areas were frequent findings. Degenerative changes were found in the nerve and ependymal cells. The so-called granulomata of Duerck, together with glial stars and larger foci of glial proliferation, were also seen frequently. Duerck granulomata were never found in subjects dying before the second day of the disease. The author does not consider them to be specific for this disease, but regards them rather as a glial reaction to haemorrhage, necrosis, degeneration of myelin, and the exudate of proteins from stagnant blood vessels. *L. Crome*

397. **The Treatment of Malaria with a Single Dose of Camoquin**
M. T. HOEKENGA. *American Journal of Tropical Medicine* [*Amer. J. trop. Med.*] **31**, 139–143, Jan., 1951. 12 refs.

"Camoquin" has the formula 4-(3′-diethylaminoethyl-4′-hydroxyanilino)-7-chloroquinoline dihydrochloride dihydrate: it was given in single oral doses in 160 cases of falciparum and 165 of vivax malaria occurring in the district of Lalima, Honduras. There were 4 unselected groups, the dosage of camoquine base being 0·4 g., 0·6 g., 0·8 g., and 1·0 g. respectively. Details of the results are given. With the falciparum cases the average duration of fever was 17·8 hours, ranging from 13·0 after the 1·0-g. dose to 18·7 hours with the 0·4-g. dose. With

the vivax cases the duration averaged 15·8 hours, all groups being essentially the same. The duration of parasitaemia in the falciparum cases was 29·2 hours, and in the vivax cases 26·4, there being no essential difference between the groups. Vivax gametocytes disappeared promptly, but falciparum gametocytes frequently persisted. Two relapses occurred, both in falciparum cases treated with 0·4 g. Toxic effects were not encountered, vomiting in 3 cases being probably due to the disease. *J. L. Markson*

398. **Clinical Prophylaxis with Proguanil and Nivaquine in a Community in Java.** [In English]
W. T. Van Goor, J. G. Lodens, and J. Alier Gomez. *Documenta Neerlandica et Indonesica de Morbis Tropicis* [*Docum. neerl. indones. Morb. trop.*] **2**, 341–349, Dec., 1950. 2 figs., 15 refs.

The results of proguanil and nivaquine (chloroquine) prophylaxis in two hyperendemic malarious villages in West Java are described. A dose of 100 to 200 mg. proguanil was given to the whole population of one village once a week for 2 years and, more recently, 200 mg. chloroquine once a week for 10 months to the population of the other village. The population at risk in each village was about the same, approximately 300 persons of all ages. During the first 6 months of proguanil therapy the parasitaemia decreased from 90 to 6% and the splenic index from 84 to 14·5%. After this both rose, the parasitaemia reaching 60% and the splenic index 58·5%. At first, the rise in parasitaemia was due to falciparum infections but later it was found that quartan infection, originally rare, had shown a remarkable increase. Thick films, which showed only 1% *Plasmodium malariae* infections at the beginning of the prophylaxis, revealed a 20% infection after 18 months. The original infection in cases with fever was shown to respond to 100 mg. proguanil daily, but *P. malariae* parasites in patients who had undergone prophylaxis resisted 300 mg. a day. In inoculation experiments the parasite was shown to resist up to 600 mg. proguanil daily. The results with 200 mg. chloroquine were excellent. Parasitaemia almost disappeared, the splenic index fell, no case of fever occurred, and so far there is no evidence of drug resistance. *William Hughes*

See also Section Hygiene and Public Health, Abstracts 4 and 5.

399. **Studies on Protozoa. Part IV. A Complement-fixation Test for Amoebiasis**
J. D. Fulton, L. P. Joyner, and I. N. O. Price. *Journal of Tropical Medicine and Hygiene* [*J. trop. Med. Hyg.*] **54**, 27–33, Feb., 1951. 12 refs.

In this paper the authors describe the methods they have used at the National Institute for Medical Research, London, to assess the value of a complement-fixation test for the diagnosis of human amoebiasis. An antigenic suspension of *Entamoeba histolytica* was prepared from a human strain cultivated with *Bacterium coli* as the only growth-promoting micro-organism present on a culture medium of the "diphasic" type, consisting of coagulated whole egg overlaid with horse-serum–Ringer solution and a small amount of sterile rice starch. [For the full technical details of the preparation and standardization of the antigen the original paper should be consulted.] Similar antigenic suspensions were prepared from *Entamoeba coli*, grown in a medium consisting of inspissated horse serum overlaid with Ringer–egg-white and in the presence of a mixed bacterial flora, and from a suspension of *Bact. coli* containing 200,000,000 bacteria per ml., heated at 56° C. for half an hour and preserved in 0·1% formol saline. When antisera produced by the injection of rabbits with the 3 antigens in increasing doses were tested against the antigens, a considerable degree of cross-fixation of complement was noted with heterologous antigens. This was thought to be due to the high antibody levels obtained by artificial immunization.

Qualitative tests were carried out on a number of human sera by allowing a single serum dilution to react with the optimum concentration of antigen and the appropriate doses of complement and of sensitized erythrocytes, the same dilution of serum, without antigen, being used as a control. A complete quantitative test, to determine the complement-fixing titre of the serum, was made when this preliminary test gave a positive result. [Full details of the technique are given, but they vary in no essential manner from the test as usually carried out.] A total of 265 human sera derived from many sources was tested in this way, and 91 reacted positively. The highest titre was 1 : 80, and the average was 1 : 10. As regards the correlation between clinical and serological findings, it is noted that *E. histolytica* had been demonstrated in the stools of 83 of these 91 patients, and that one other had suffered from amoebiasis a year previously. Of the 174 negative reactors, 142 gave no clinical history suggestive of amoebiasis, but the remaining 32 showed either clinical or pathological signs of infection. Parallel tests with *Entamoeba coli* were made in 38 instances, and gave the following results:

Antigen	Positive Sera	Negative Sera
E. histolytica	23	15
E. coli	2	36

The significance of the positive results with *E. coli* is uncertain, because each serum reacted to the same titre with both species.

These results confirm the findings of other workers that specific antibodies are present in the serum of many patients harbouring *E. histolytica*. As in other infections in which serological tests are used for diagnosis, false positive and false negative reactions may occur. Complement-fixation tests are not likely to be of much value in primary diagnosis, or in surveys of infection rates among the general population. They have, however, a potential value in the assessment of the results of treatment, and in providing evidence about the cause of hepatitis or liver abscess. The authors consider, however,

that further investigations should be carried out in an endemic area, and that attempts should be made to improve the quality of the antigens used in the test, so that its real value can be established.

J. C. Broom

400. **Indigenous Amoebiasis in Britain**
T. C. MORTON, R. A. NEAL, and M. SAGE. *Lancet* [*Lancet*] **1**, 766–769, April 7, 1951. 3 figs., 12 refs.

The authors examined 1,000 R.A.F. apprentices, none of whom had been out of Britain, for the presence of *Entamoeba histolytica*. The incidence was found to be 1·6%, as compared with 8.8% found in R.A.F. personnel invalided home with diseases other than dysentery. Seven of the infections found in the apprentices were of the large race, 8 were of the small race, and one was a mixed infection. Four of the large-race strains were potentially pathogenic, since on inoculation into young rats the resulting infections ulcerated the caecum. Infections with two other strains of the large race were obtained in rats, but no lesions were observed. Sigmoidoscopy in 2 of the infected apprentices showed a normal mucosa in both.

The authors describe 3 cases of amoebic dysentery, one fatal, in R.A.F. personnel who had never left Britain. *R. A. Neal*

RHEUMATIC INFECTIONS

401. **Rheumatic Fever and Glomerulonephritis. A Clinical and Postmortem Study**
S. A. HARTMAN and E. F. BLAND. *American Journal of Medicine* [*Amer. J. Med.*] **10**, 47–51, Jan., 1951. 28 refs.

The association of rheumatic fever and glomerulonephritis has been investigated in 117 patients suffering from glomerulonephritis and in 188 post-mortem records of cases of rheumatic carditis. In the former series there was a total incidence of 6% of polyarthritis or rheumatic heart disease, and in 2·5% active rheumatism and nephritis co-existed. From records of the cases of rheumatic carditis it was found that 5 of the subjects had had acute glomerulonephritis at death, 4 chronic nephritis, and 7 a proliferation of glomerular epithelium, but not sufficient to warrant the diagnosis of glomerulonephritis. *Henry Cohen*

402. **Acetylsalicylic Acid and Urinary Excretion of Adrenocortical Steriods**
H. VAN CAUWENBERGE and C. HEUSHGEM. *Lancet* [*Lancet*] **1**, 771–773, April 7, 1951. 7 refs.

This is a preliminary report on the study of the effect of acetylsalicylic acid on the urinary excretion of adrenocortical steroids in 8 patients suffering from "collagen" diseases—rheumatic fever, rheumatoid arthritis, ankylosing spondylitis, and fibrositis with endarteritis. Before treatment all patients had a low output of reducing steroids. With salicylates excretion was markedly raised, but fell at once on cessation of treatment. An increased output of reducing steroids was associated with clinical improvement. No regular variation was found in the excretion of 17-ketosteroids during salicylate therapy, and variations in excretion were not correlated with the clinical course.

The results suggest a relation between salicylate and cortisone therapy. *H. F. Turney*

403. **Salicylate, Gentisate, and Circulating Eosinophils**
B. W. MEADE and M. J. H. SMITH. *Lancet* [*Lancet*] **1**, 773–774, April 7, 1951. 14 refs.

The effect of single doses of sodium salicylate and sodium gentisate on the circulating eosinophils has been studied in normal healthy subjects. No significant depression was observed with plasma-salicylate concentrations up to 38 mg. per 100 ml. and plasma-gentisate concentrations up to 35 mg. per 100 ml.—[Authors' summary.]

404. **A Quantitative Study of Salicylate Therapy in Rheumatic Fever.** (Quantitative Untersuchungen zur Salizyltherapie des rheumatischen Fiebers)
W. BLUMENCRON and E. BORKENSTEIN. *Medizinische Welt* [*Med. Welt*] **20**, 275–279, March 3, 1951. 2 figs., 10 refs.

Efficient salicylate therapy of rheumatic fever depends on correct selection of cases and an adequate level of the substance in the blood. The minimum level is 35 mg. per 100 ml. of blood and must be reached quickly and maintained for some time. The rapid increase necessary can only be obtained by intravenous therapy.

The attainment of an effective blood level depends essentially on the degree of intolerance. Symptoms of indigestion prevent peroral exhibition of single doses as large as 2 g. or daily doses over 8 g., while such therapy for more than 3 days is generally impossible. Salicylate may be given successfully per rectum as an isotonic solution or in gruel in order to diminish the local irritation. By the rectal route single doses of up to 8 g. in isotonic solution or 5 g. in gruel, and daily doses of up to 16 g. (divided into two or three parts), can be given. By this means maintenance of an effective blood level is possible. By intravenous therapy only 2 g. in 10% solution can be given as a single dose. Repeated injection of 1 g. sodium salicylate, however, produces an effective blood level. The ethanolamine salt of salicylic acid gives a more persistent blood level with correspondingly fewer injections. The diminution of gastric upset when sodium bicarbonate is given is of no value, for the blood level remains low owing to increased excretion.

Ideal blood levels may be obtained with an initial intravenous dose followed by maintenance by the rectal route. On subsidence of the acute stage, peroral therapy may be instituted. Observation of the serum salicylate level is essential in salicylate medication because the drug as a rule should be administered until the limits of tolerance are reached. *Norval Taylor*

405. **Rheumatic Fever Treated with Cortisone and ACTH**
J. D. KEITH and C. A. NEILL. *Canadian Medical Association Journal* [*Canad. med. Ass. J.*] **64**, 193–198, March, 1951. 8 figs., 6 refs.

History of Medicine

406. **The History and Development of Forensic Medicine**
S. SMITH. *British Medical Journal* [*Brit. med. J.*] **1**, 599–607, March 24, 1951.

Defining forensic medicine as " that body of medical and paramedical scientific knowledge which may be used for the purposes of administration of the Law ", the author briefly reviews its history from early Egyptian times, Imhotep, Grand Vizier, Chief Justice, and Physician to King Zozer, being the first known medico-legal expert. Modern forensic medicine was, however, born in the 18th century in Germany, where a number of chairs of state or forensic medicine were founded and pioneers like Plenck (1781) and Metzger (1793) published their authoritative works. France soon followed the lead of her neighbour, chairs were established at Paris, Strasbourg, and Montpellier, and Fodéré published his great treatise (1796).

In Great Britain, Samuel Farr published the first comprehensive work on the subject (1788). Andrew Duncan, senior, of Edinburgh, began lecturing on medical jurisprudence and public hygiene about 1789, and he presented a Memorial on the subject to the Patrons of Edinburgh University in 1798. As a result of Government interest in the matter, the Crown created the first British chair of medical jurisprudence at Edinburgh in 1807, the first incumbent of the new chair being Duncan's son, Andrew Duncan *secundus*. Chairs were later founded at London (1834), Glasgow (1839), and Aberdeen (1857). In the U.S.A. progress was uneven, but the first chair was founded there in 1813 at New York.

With the development of specialization in modern times, forensic medicine has been split up, and forensic pathology, serology, and toxicology have been evolved. The great need of the present time, in the author's opinion, is the provision of establishments or institutes where specialists in these fields can operate as a team when necessary. *H. P. Tait*

407. **Glinski and the Aetiology of Simmonds's Disease (Hypopituitarism)**
J. D. ROBERTSON. *British Medical Journal* [*Brit. med. J.*] **1**, 921–923, April 28, 1951. 15 refs.

408. **The Development of Public Health Services in a Rural County: 1838–1949**
M. I. ROEMER and B. FAULKNER. *Journal of the History of Medicine and Allied Sciences* [*J. Hist. Med.*] **6**, 22–43, Winter, 1951. 20 refs.

409. **The History of Quarantine in Britain during the 19th Century**
J. C. MCDONALD. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **25**, 22–44, Jan.–Feb., 1951. Bibliography.

410. **Social Medicine and the Epidemic Constitution**
I. GALDSTON. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **25**, 8–21, Jan.–Feb., 1951. 19 refs.

411. **Primitive Medical Art and Primitive Medicine-men in Australia**
L. P. WINTERBOTHAM. *Medical Journal of Australia* [*Med. J. Aust.*] **1**, 461–468, March 31, 1951. 7 figs., 11 refs.

412. **A History of Anatomy at Glasgow University**
R. MITCHELL and J. C. WARBRICK. *Surgo, Glasgow University Medical Journal* [*Surgo, Glasg.*] **17**, 71–77, 1951. 4 figs.

413. **The Early History of Radium in London**
C. E. IREDELL. *Proceedings of the Royal Society of Medicine* [*Proc. R. Soc. Med.*] **44**, 207–209, March, 1951.

414. **Giordano Bruno: the Philosophy of Circles and the Circular Movement of the Blood**
W. PAGEL. *Journal of the History of Medicine and the Allied Sciences* [*J. Hist. Med.*] **6**, 116–124, Winter, 1951. 5 figs., 14 refs.

415. **Dr. Ibis and the Artists: a Sidelight upon Hunter's Atlas, *The Gravid Uterus***
B. C. CORNER. *Journal of the History of Medicine and the Allied Sciences* [*J. Hist. Med.*] **6**, 1–21, Winter, 1951. 2 figs., 32 refs.

416. **Epilation through the Ages.** (L'épilation à travers les âges)
L. GRANT. *Journal des Praticiens* [*J. Prat., Paris*] **65**, 46–50, Jan. 18, 1951. 19 refs.

417. **The Evolution of the Gynaecologist**
A. L. ROBINSON. *Journal of Obstetrics and Gynaecology of the British Empire* [*J. Obstet. Gynaec. Brit. Emp.*] **58**, 50–72, Feb., 1951. 9 figs.

418. **The English Military Surgeon 1603–1641**
D. STEWART. *Journal of the Royal Army Medical Corps* [*J. roy. Army med. Cps*] **96**, 46–56, Jan., 1951.

419. **Military Surgery in the First Empire.** (La chirurgie militaire sous le premier empire)
R. VAULTIER. *Presse Médicale* [*Pr. méd.*] **59**, 413–416, March 28, 1951. 10 figs.

420. **First Successful Pylorectomy for Cancer. The Case History**
A. BRUNSCHWIG and E. SIMANDL. *Surgery, Gynecology and Obstetrics* [*Surg. Gynec. Obstet.*] **92**, 375–379, March, 1951. 2 figs.

BIOGRAPHY

421. **The Hunterian Heritage**
M. PAGE. *British Medical Journal* [*Brit. med. J.*] **1**, 489–496, March 10, 1951. 4 figs., 12 refs.

The salient facts of Hunter's life are reviewed, and the comments, kind and unkind, of his contemporaries are related to the conditions of the time. The later evaluation of Hunter shows the same uneven appreciation of his worth as was held by his contemporaries. Fresh emphasis is laid on Hunter's enterprise and business ability, which allowed a man as ignorant of finance as most doctors are, and often impecunious, to accumulate an invaluable museum, an experimental country farm, and an ambitious town house with private lecture gallery and museum.

The experimental tradition of Hunter must remain the basis of new knowledge, but the Royal College of Surgeons in the new conditions in which it finds itself, with an attached post-graduate college, now has virtual monopoly of English surgical education. A plea for the practical side of training is made. Gibbon observed that of the two educations that a man had, the one given him and the one he gave himself, the second was by far the more important. Lectures impart knowledge but cannot give wisdom, and specialties, by fragmenting the profession, weaken its unity. Duke-Elder, in 1945, asked "if the practice of medicine becomes more and more an affair of the State, is the profession provided with a body powerful enough to preserve the soul of medicine in its personal and creative aspects, without which it cannot live?" There is need for linking together the existing traditional organizations to obtain this greater strength and greater professional unity.

J. G. Bonnin

422. **Dublin's Surgeon-anatomists**
W. DOOLIN. *Annals of the Royal College of Surgeons of England* [*Ann. R. Coll. Surg. Engl.*] **8**, 1–22, Jan., 1951. 6 figs., 42 refs.

The Dublin Guild of Barber Surgeons was founded in 1446 by Henry VI of England to provide treatment for those of his army who were wounded in the defence of Dublin, the bridgehead first established by the Norman invader in the 12th century. This was the earliest recognition by the monarchy of the surgical craft, and preceded the establishment of similar Guilds in London and Edinburgh later in the fifteenth century. The Irish were for long banned from membership, and even up to the eighteenth century it was ruled that apprentices must be of the Protestant religion. The influence of the Normans can be seen in the fact that the profession was in the hands of barbers and smiths. Later the Guild was replaced by the Dublin Society of Surgeons (1780), and this finally became a Royal College by charter in 1784. The University of Dublin was founded independently by Queen Elizabeth in 1591, but it was not until 1711 that the School of Physic was established at Trinity College.

Among the more eminent surgeon anatomists of Dublin was Fielding Ould, who succeeded Bartholomew Mosse, the founder and first Master of the Rotunda, after studying midwifery under Mauriceau in Paris, and later became famous as the author of the standard English treatise on midwifery. Other notable figures of the eighteenth century were George Cleghorn, a gifted teacher, and Sylvester O'Halloran, who had studied for a time in Paris where, under the patronage of Louis XIV, rapid progress was being made in surgery. He returned to Ireland to suggest a far-sighted scheme of reform, including the establishment of new chairs in surgery, operative surgery, and anatomy, a register of surgeons, and free medical education.

The beginning of the nineteenth century saw Abraham Colles as President of the Royal College of Surgeons of Ireland. A close friend of Sir Astley Cooper, whom he assisted in his anatomical study of hernia, his accurate observations of the plane of the perineal fascia, the radial fracture, and the breast of the infected foster mother brought him lasting fame. Appointed Professor of Anatomy in 1804, he was essentially the surgeon-anatomist, emphasizing the subservience of anatomy to the operator's need, and in this he was in marked contrast to his contemporary, James Macartney, the gifted anatomist and inspiring teacher who, in 1813, became Professor of Surgery in Dublin University and was largely responsible for raising the Dublin school to the level of those of London and Edinburgh. An energetic extravert who would demonstrate to his students how to tie the femoral artery blindfold or to ligature the vessel with his back to the body, this disputatious, self-opinionated man dominated the Dublin school for 26 years and numbered among his pupils such men as Jones Quain (of Quain's "Anatomy") and Benjamin Alcock (of "Alcock's canal"), who became the first Professor of Anatomy at University College, Cork.

[This paper contains many illuminating digressions on such matters as the Battle of the Boyne, the sights of Dublin, the persecution of the Irish, and the birth of the Duke of Wellington.] *Ruth Hodgkinson*

423. **Robert Liston (1794–1847)**
A. L. SCHOFIELD. *British Journal of Plastic Surgery* [*Brit. J. plast. Surg.*] **3**, 227–232, Jan., 1951. 13 refs.

Rapidity and dexterity in operating were the outstanding qualities which Liston brought to surgery. This skill, which brought him eminence in the pre-anaesthetic era when "the quicker the surgeon the greater the surgeon", was based on a thorough mastery of anatomical detail and a careful attention to technique. His knowledge of anatomy, acquired first as a pupil of, and later as assistant to, the famous anatomist, John Barclay (1758–1826), was further extended when he opened a school of anatomy with the help of his cousin, James Syme (1799–1870), Professor of Clinical Surgery at Edinburgh and chiefly remembered for the amputation which bears his name. On the other hand, he was not above learning technique from Edinburgh butchers, while physical strength was another valuable addition to his surgical armamentarium.

Surgeons of the early nineteenth century operated on every system and every part of the body, and Liston

was a general surgeon in the widest sense of the term, excelling in such diverse fields as lithotomy, orthopaedics. and plastic surgery, to which last field he made considerable contributions. In 1827, 1831, and again in 1834–5 he published clinical notes on patients treated by rhinoplasty by the Indian method, using his own technique for reconstruction of the columna. His bold surgical approach to tumours of the mouth and jaws included hemisection of the maxilla and mandible, while for epispadias he devised an operation consisting in " paring the edges thoroughly, and putting them together over a catheter by the introduction of many points of twisted suture ". Liston's claim to fame, however, lies not so much in his originality as in his boldness and unsurpassed technical skill.

[Brief mention only is made in this article of the fact that Liston recognized the surgical possibilities of anaesthesia, and was the first surgeon in Britain to perform a major operation under ether. He was, in fact, the first to make use of the basic revolution in surgical practice of his day, a revolution which was to obviate the necessity of rapid operating of which he was a master. Possibly this was his greatest contribution to reconstructive surgery, which benefited immensely from the reorientation in surgical practice to which he gave his support.] *Ruth Hodgkinson*

424. **Henry Maudsley: his Work and Influence**
A. LEWIS. *Journal of Mental Science* [*J. ment. Sci.*] **97**, April, 1951.

Henry Maudsley (1835–1918) was born of yeoman stock in the West Riding of Yorkshire and received his medical training at University College Hospital, London, where, in 1850, he was apprenticed to Clover, then Resident Medical Officer. His entry into psychiatric work was accidental, for when he went to do 6 months' service in the asylum at Wakefield he did so merely to fulfil the conditions for an appointment with the East India Company. So strongly was he attracted by work with the mentally ill that he went from Wakefield to Brentwood, and thence to Cheadle Royal, Manchester, where, at the age of 23, he was made Medical Superintendent. In that post he was an outstanding success and during his 3 years there he developed most of the ideas which he was to spend the rest of his life in propagating, chief amongst them being the view that insanity is a bodily disease and that no disgrace should be attached to it. His ideas and opinions were revolutionary in 1860, and even to-day many of them are still thought to be new.

Maudsley was widely read in the science and philosophy of his day. A philosophical inquirer, he was a positivist to whom metaphysics was anathema. In his first published article (*J. ment. Sci.*, 1859) he stated that " man's consciousness and moral nature and all his other psychological attributes are closely dependent on the physical structure of his brain ", and this view was maintained in his last work, " Organic to Human ", nearly 60 years later. In his implicit belief in progress and in his assumption that moral principles are laws of nature Maudsley was typical of his age, but he differed from it in his attitude towards the insane, with whom, unlike Hughlings Jackson, he felt a sympathetic kinship. The publication of his treatise " The Physiology and Pathology of Mind " (1867) was a turning point in the history of English psychiatry, for it made him the first English psychiatrist to command a following outside his own country.

Maudsley's best memorial is the hospital which bears his name. He had long advocated the creation of a psychiatric hospital devoted to early treatment, research, and postgraduate teaching, and when a similar project was proposed in 1907 by his former pupil Sir Frederick Mott, then Pathologist to the London County Council Mental Hospitals, he offered to give £30,000 towards the building of such a hospital, subject to its association with the University of London, an offer which was accepted at once. After some delay, the building was completed in 1915, and although it was not fully opened until 1923, Maudsley, before his death in 1918, was able to see some of its work started under Mott's direction.

[The above is a purely factual summary; the paper should be read in its entirety for the author's lucid exposition of Maudsley's ideas.] *F. H. L. Poynter*

425. **Michael Servetus and the Pulmonary Transit of the Blood**
R. H. BAINTON. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **25**, 1–7, Jan.–Feb., 1951. 11 refs.

426. **Marcello Malpighi. I. Malpighi and the Public Study of Anatomy in Bologna.** (Studi e richerche su Marcello Malpighi. Nota I. Malpighi e la funzione pubblica dell'anatomia a Bologna)
A. GALLASSI. *Rivista di Storia delle Scienze Mediche e Naturali* [*Riv. Storia Sci. med. nat.*] Suppl. 1, **41**, 7–28, 1950. 34 refs.

427. **Henri IV and his Physicians.** (Henri IV et ses médecins)
R. VAULTIER. *Presse Médicale* [*Pr. méd.*] **59**, 242–244, Feb. 21, 1951. 7 figs.

428. **Francis R. Packard and his Role in Medical Historiography**
W. B. MCDANIEL. *Bulletin of the History of Medicine* [*Bull. Hist. Med.*] **25**, 66–85, Jan.–Feb., 1951. 1 fig., 3 refs.

429. **Reginald Heber Fitz's Contribution to the Development of Medical Education and Practice in America**
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